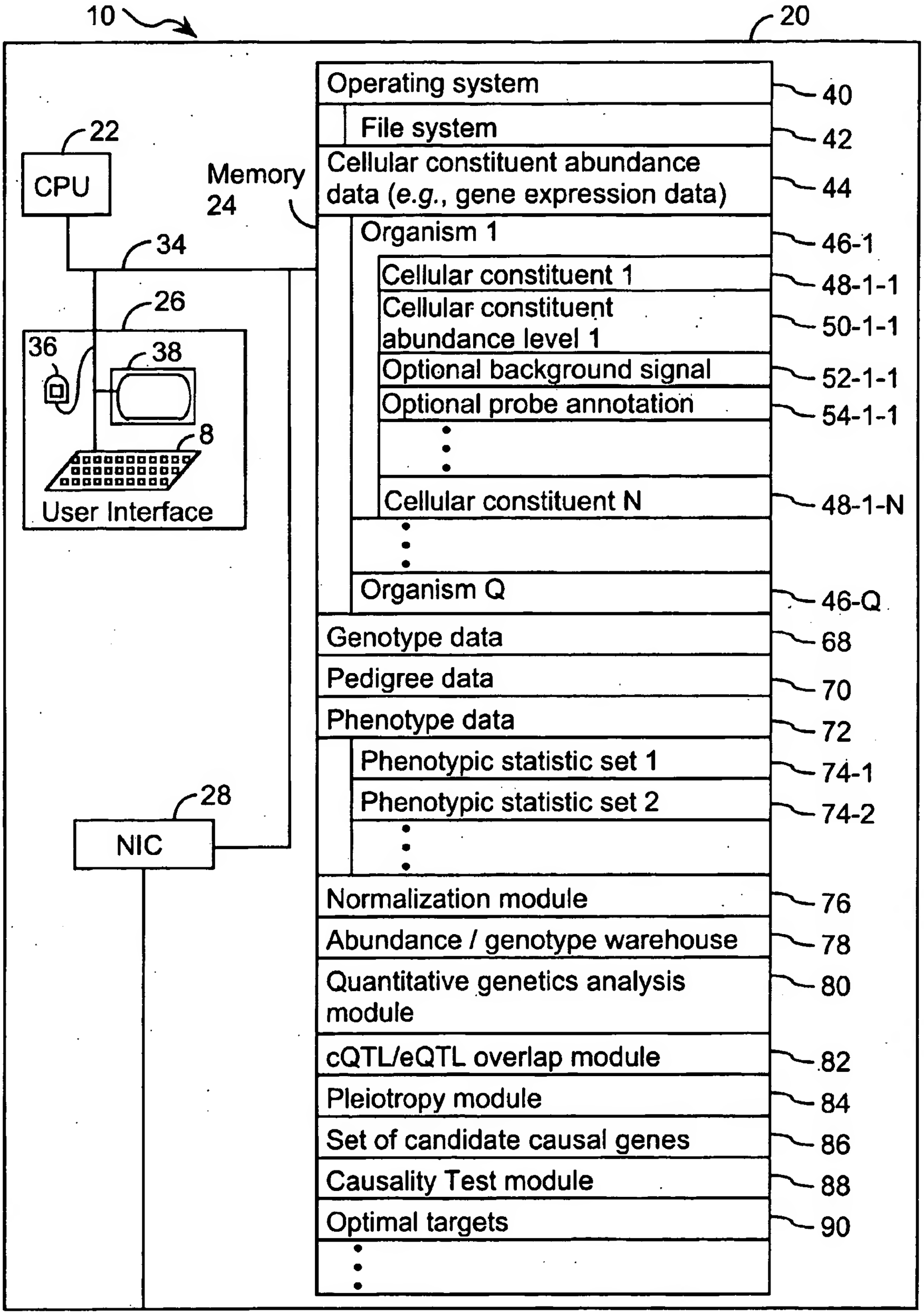

10
20
Operating system
40
File system
42
Cellular constituent abundance data (e.g., gene expression data)
44
Organism 1
46-1
Cellular constituent 1
48-1-1
Cellular constituent abundance level 1
50-1-1
Optional background signal
52-1-1
Optional probe annotation
54-1-1
Cellular constituent N
48-1-N
Organism Q
46-Q
Genotype data
68
Pedigree data
70
Phenotype data
72
Phenotypic statistic set 1
74-1
Phenotypic statistic set 2
74-2
Normalization module
76
Abundance / genotype warehouse
78
Quantitative genetics analysis module
80
cQTL/eQTL overlap module
82
Pleiotropy module
84
Set of candidate causal genes
86
Causality Test module
88
Optimal targets
90
22
CPU
Memory 24
34
26
36
38
8
User Interface
28
NIC

FIG. 1

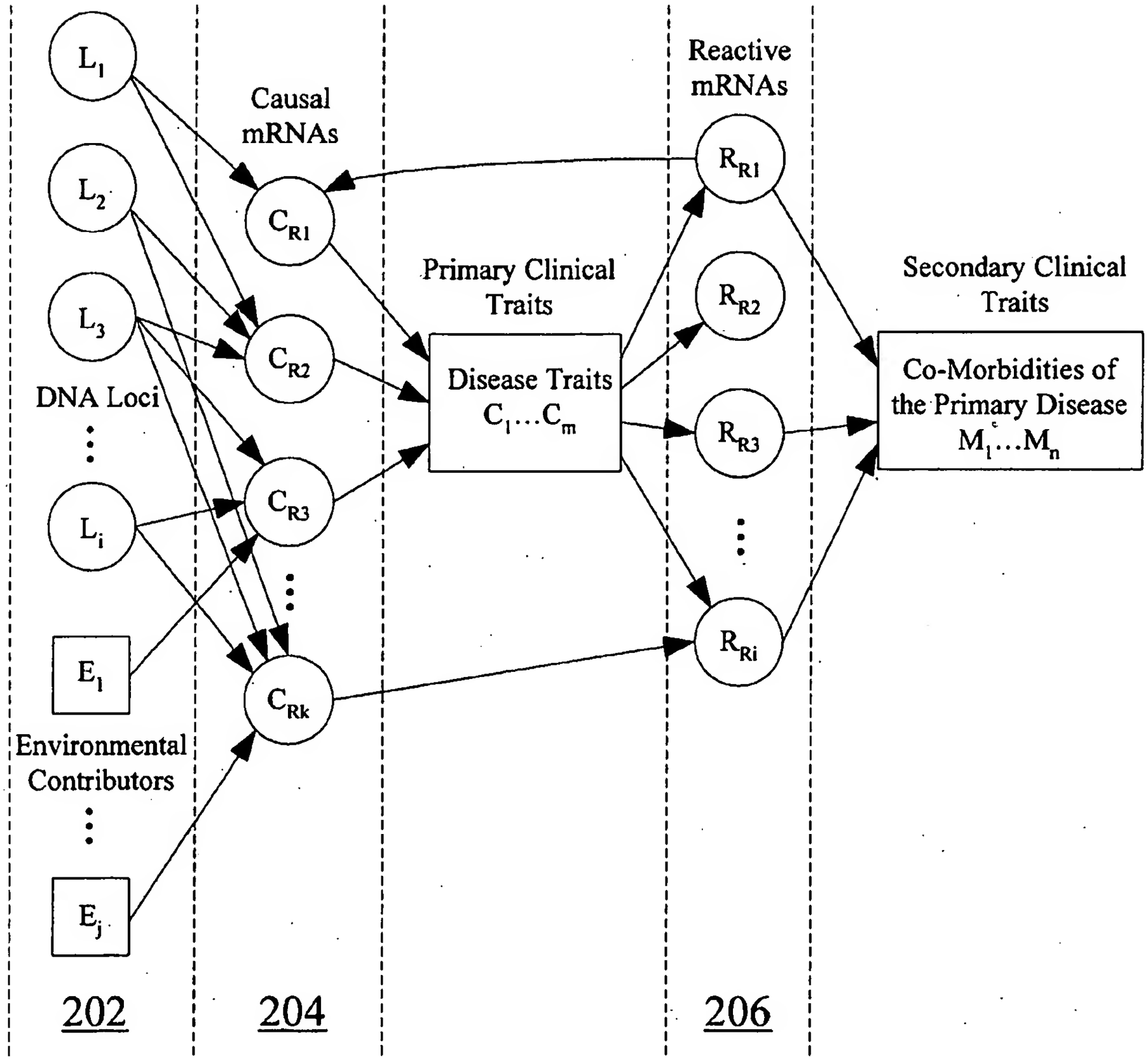

L1
L2
L3
DNA Loci
Li
E1
Environmental Contributors
Ej
Causal mRNAs
CR1
CR2
CR3
CRk
Primary Clinical Traits
Disease Traits C1...Cm
Reactive mRNAs
RR1
RR2
RR3
RRi
Secondary Clinical Traits
Co-Morbidities of the Primary Disease M1...Mn
202
204
206

Fig. 2

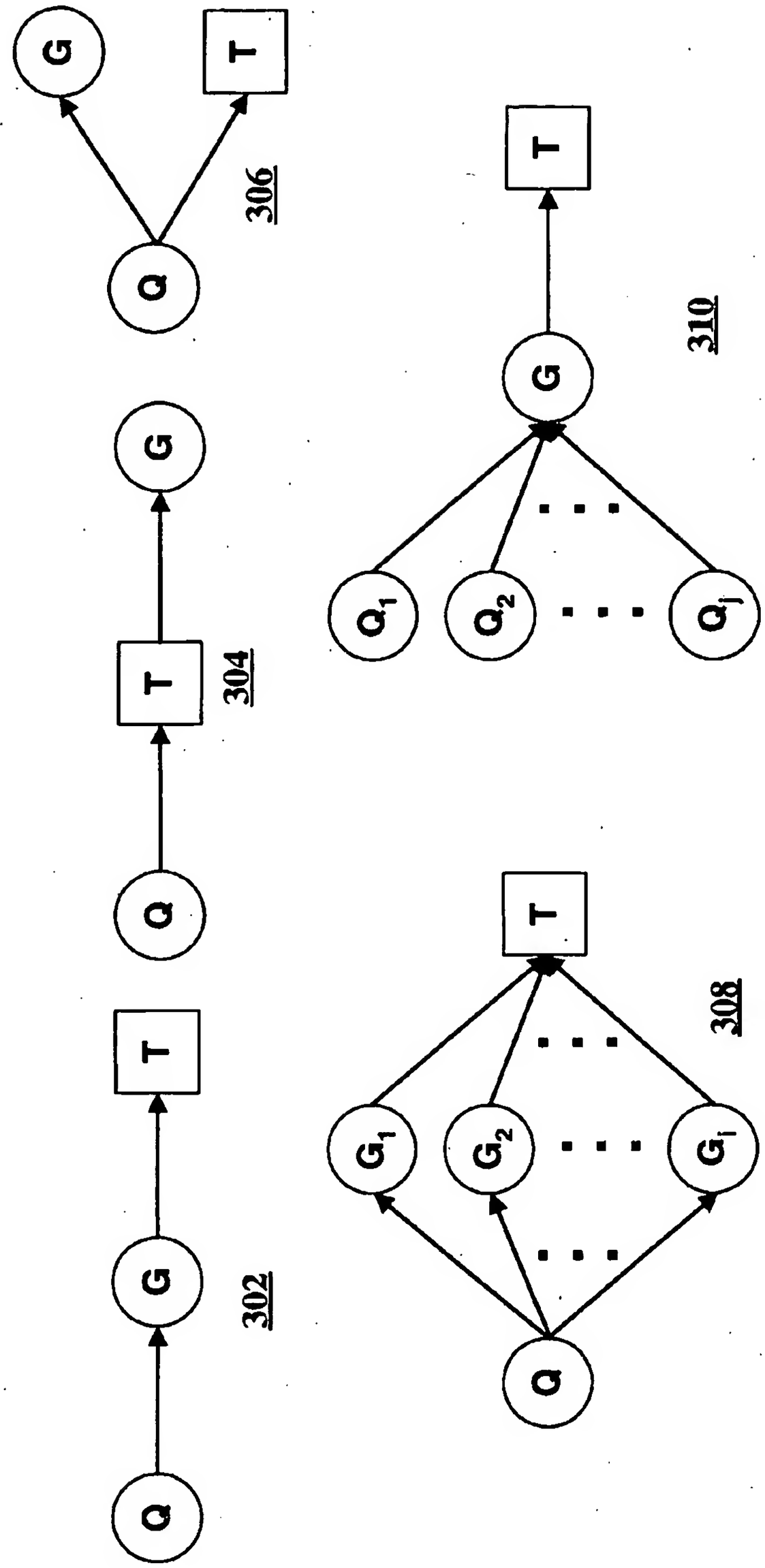


Fig 3A

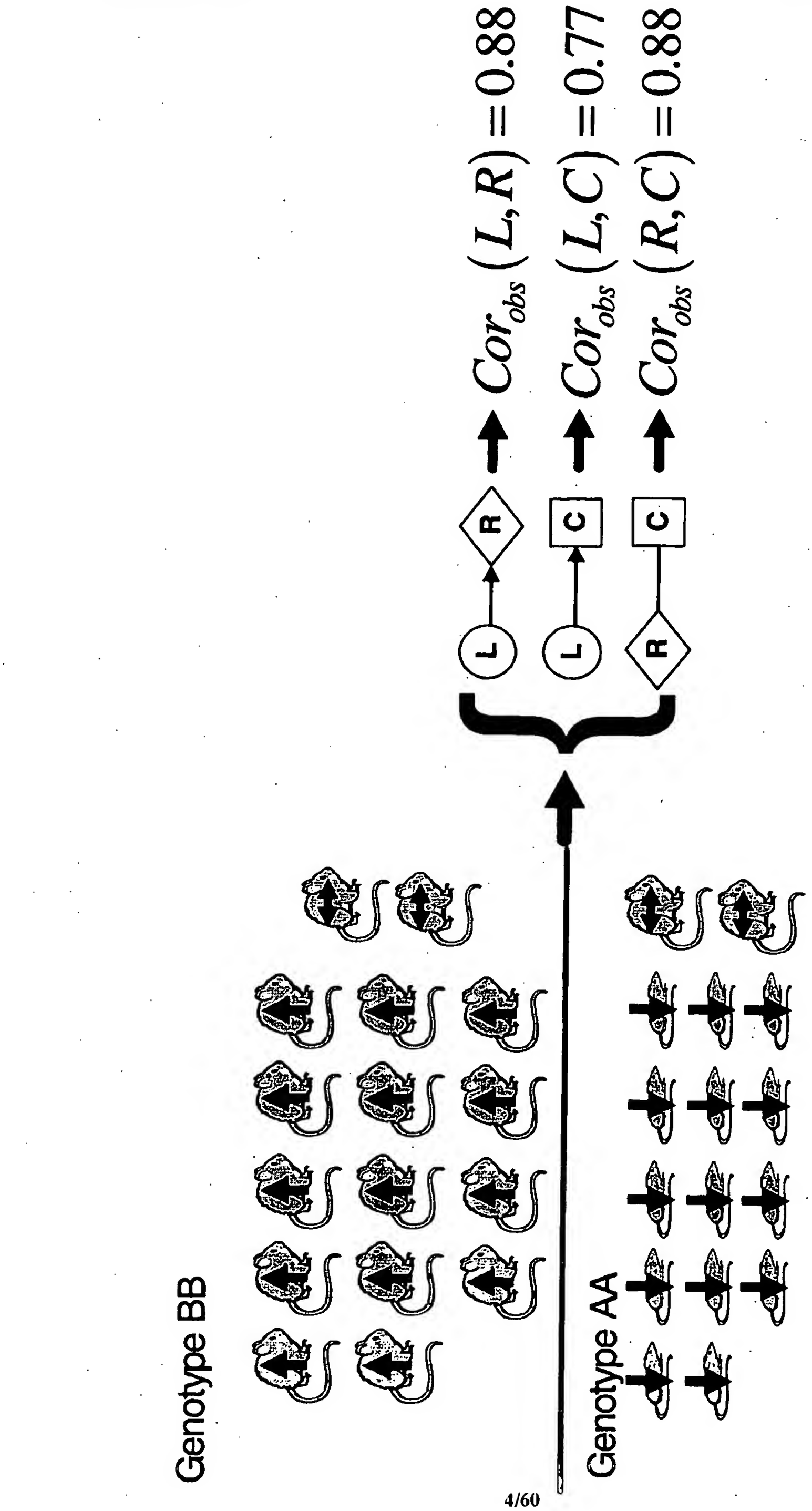

$Cor_{obs}(L,R) = 0.88$
$Cor_{obs}(L,C) = 0.77$
$Cor_{obs}(R,C) = 0.88$
R
C
C
L
L
R
Genotype BB
Genotype AA

Figure 3B

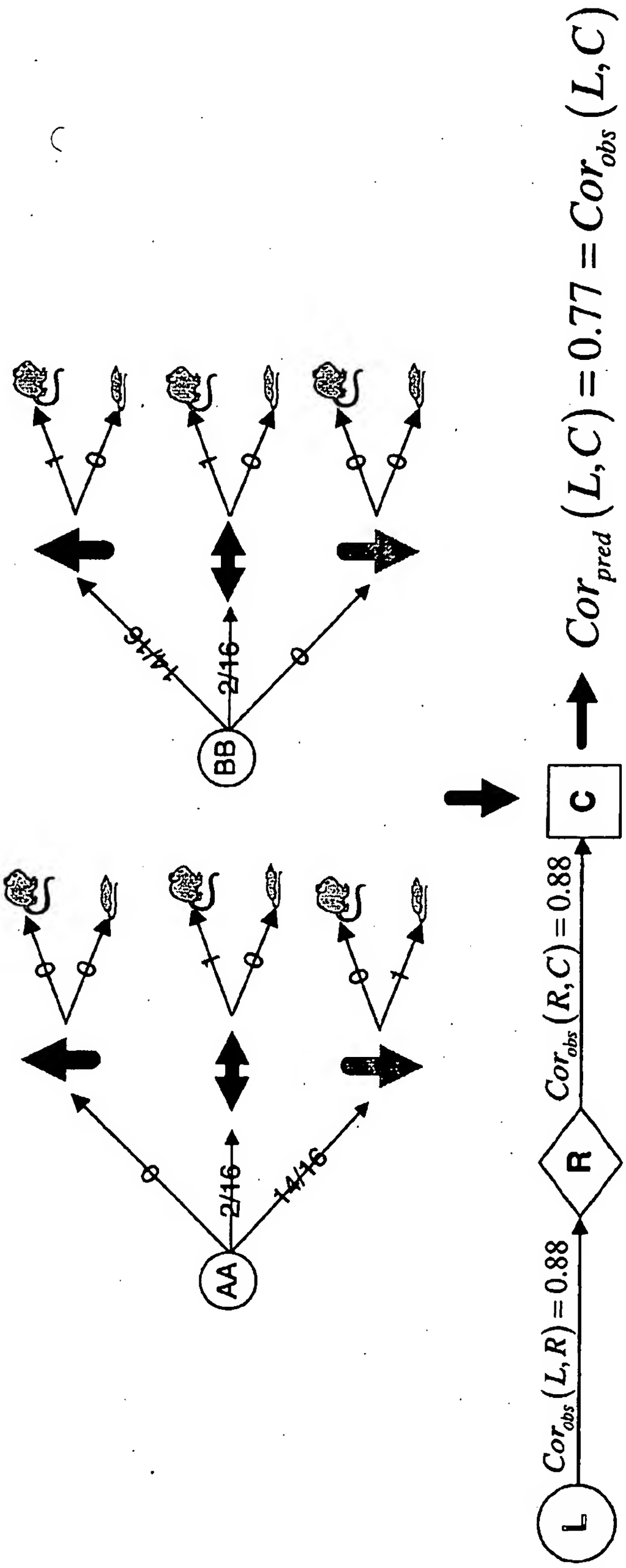
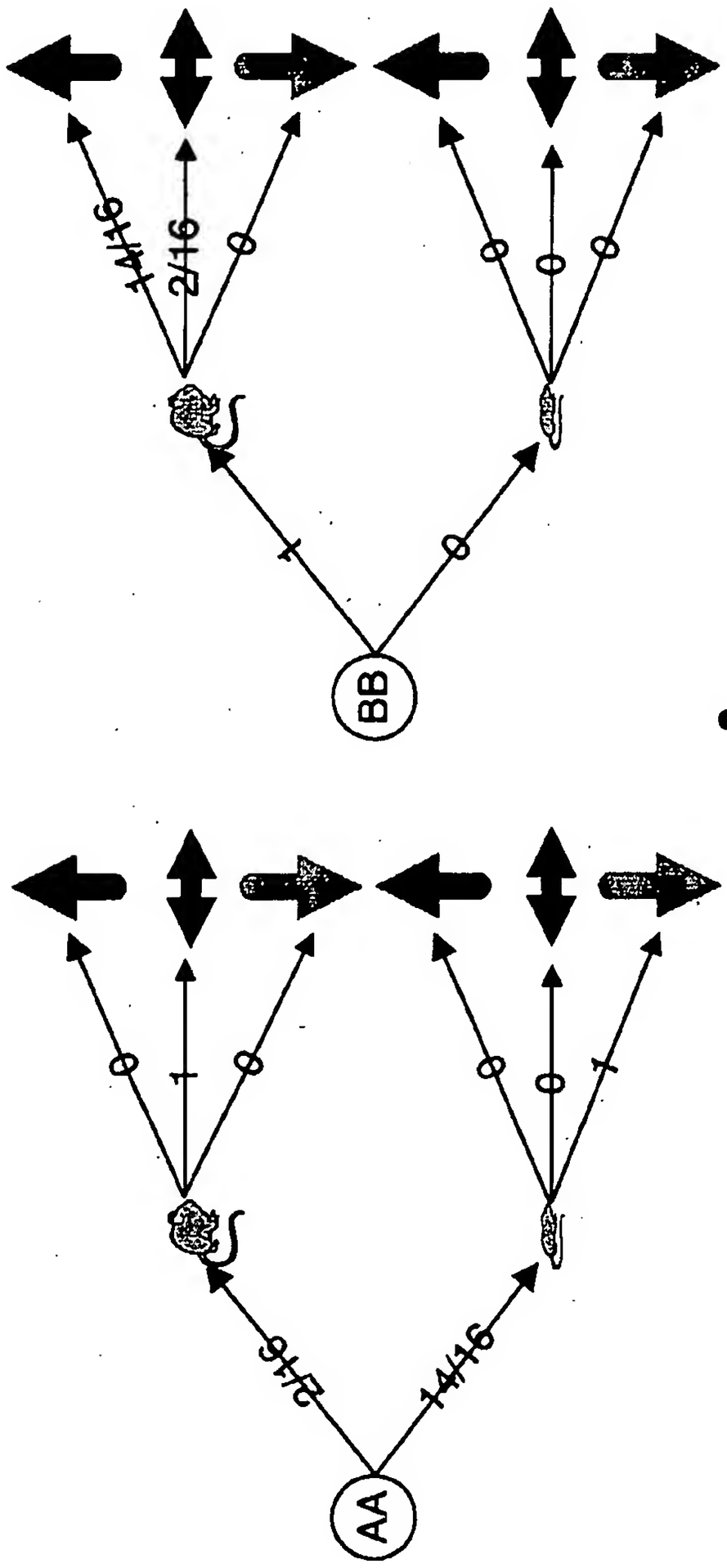

AA
2/16
14/16
0
BB
2/16
14/16
0
$Cor_{obs}(L,R) = 0.88$
L
R
$Cor_{obs}(R,C) = 0.88$
C
$Cor_{pred}(L,C) = 0.77 = Cor_{obs}(L,C)$

Figure 3C


1
2/16
0
BB
0
0
0
1
0
AA
14/16
2/16

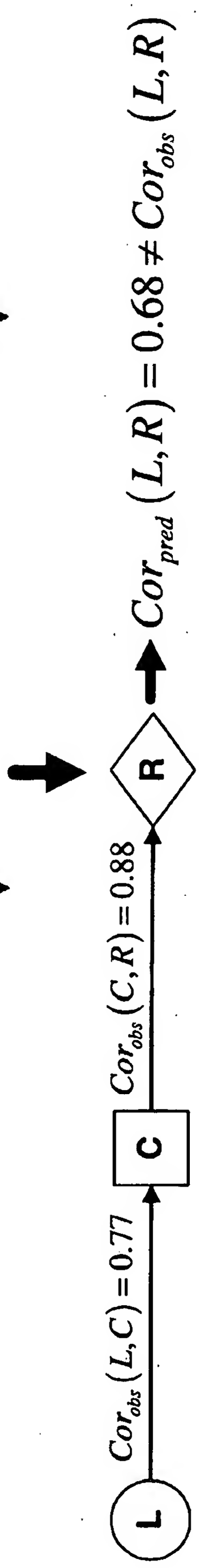

$Cor_{obs}(L,R) = 0.68 \neq Cor_{obs}(L,R)$
$Cor_{pred}(L,R)$
R
$Cor_{obs}(C,R) = 0.88$
C
$Cor_{obs}(L,C) = 0.77$
L

Figure 3D

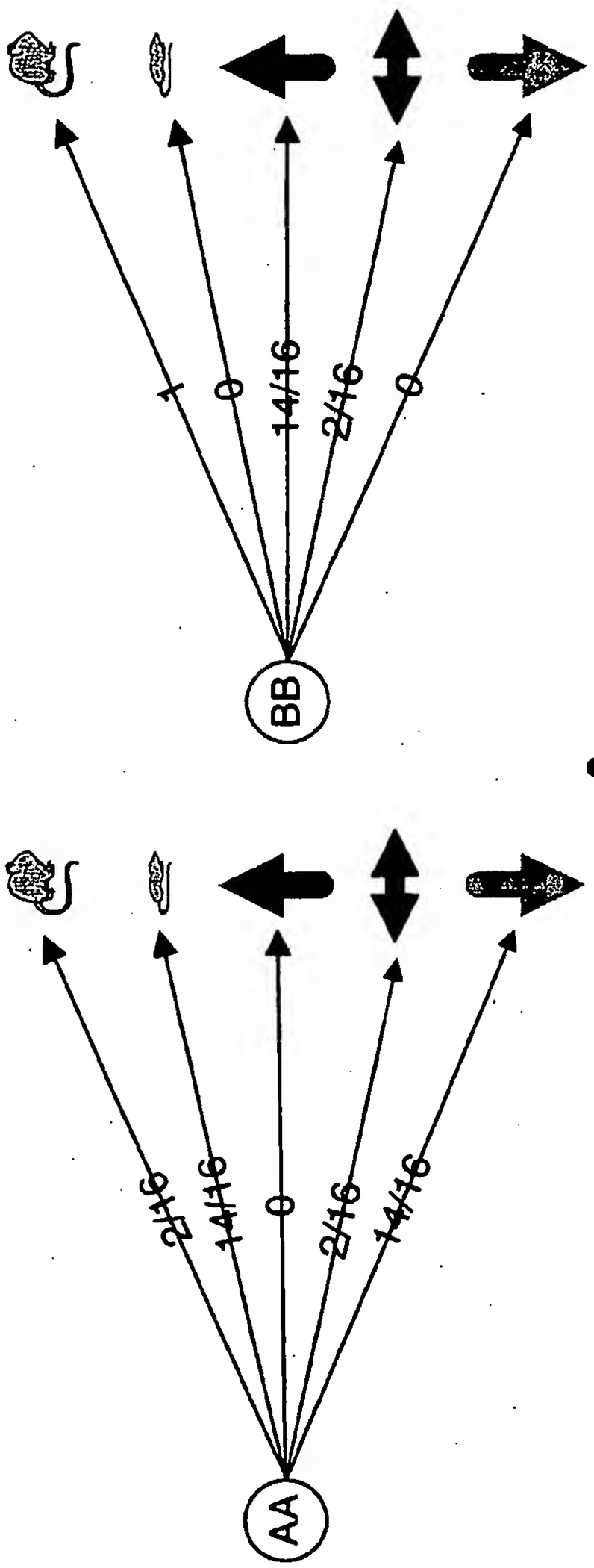

1
0
14/16
2/16
0
BB
2/16
14/16
0
2/16
14/16
AA
0.88
L,R
Cor_{obs}
0.77
L,C
Cor_{obs}
R
C
L
$Cor_{pred}(R,C) = 0.68 \neq Cor_{obs}(R,C)$

Figure 3E

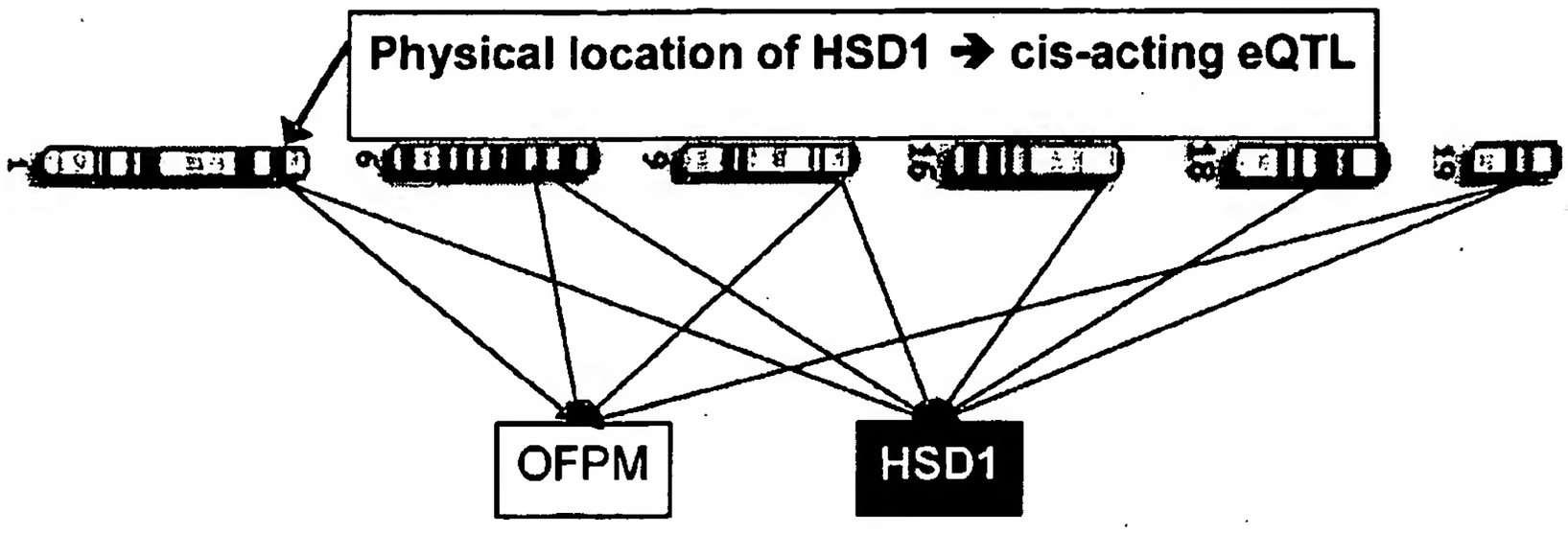

Physical location of HSD1 → cis-acting eQTL
OFPM
HSD1

Fig. 4.

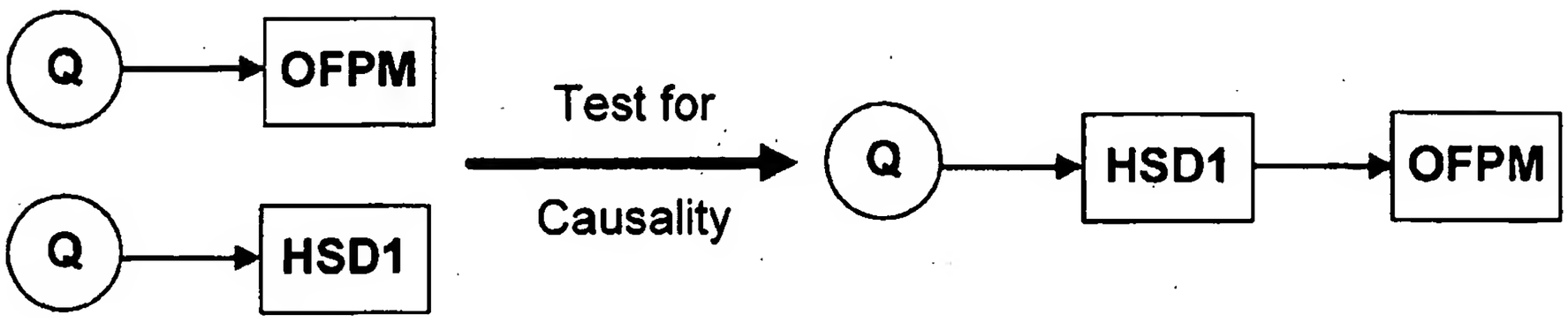
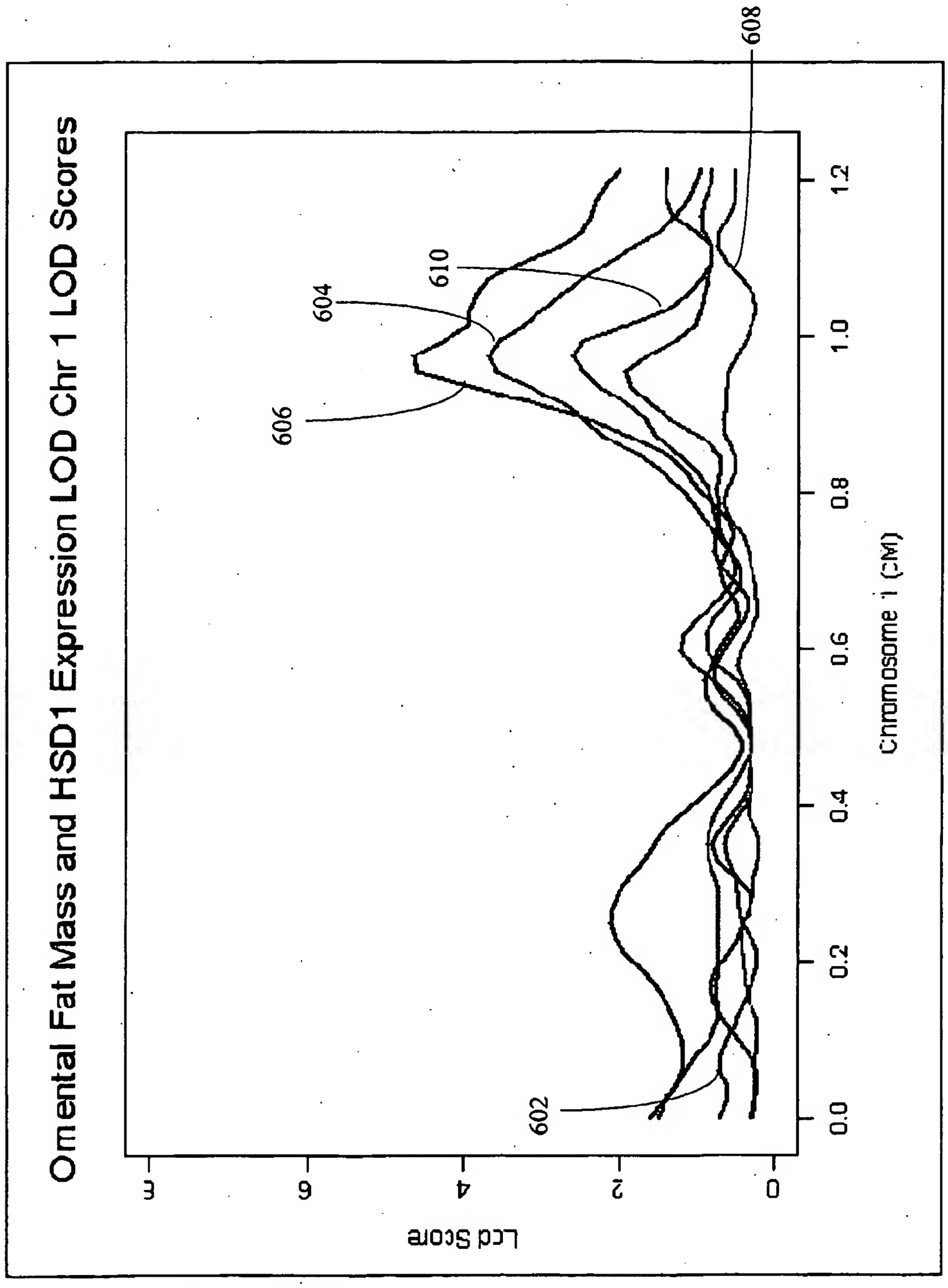

Q
OFPM
Q
HSD1
Test for
Causality
Q
HSD1
OFPM

Fig. 5



Chromosome 6 (cM)

Fig. 6

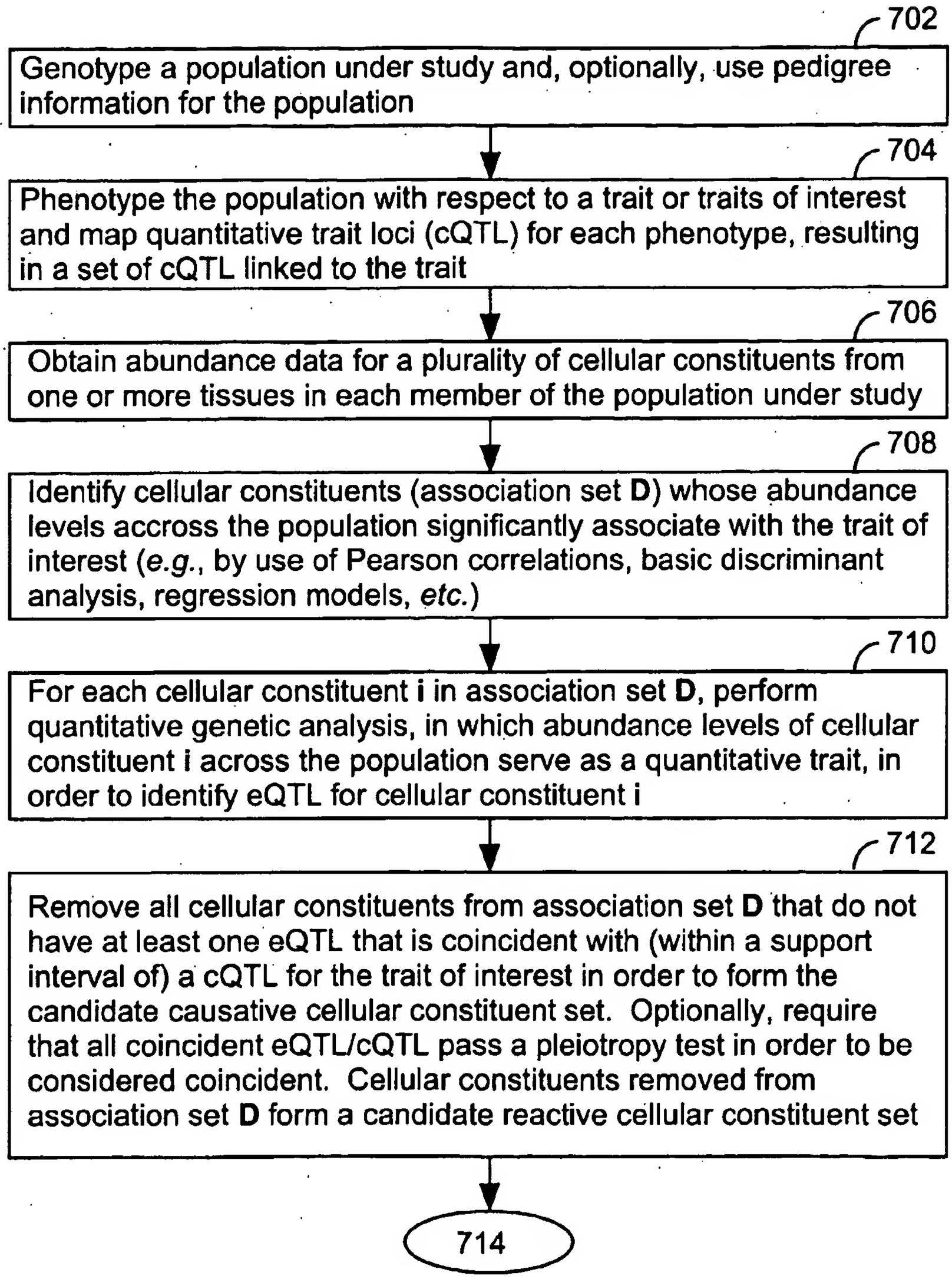

702
Genotype a population under study and, optionally, use pedigree information for the population
704
Phenotype the population with respect to a trait or traits of interest and map quantitative trait loci (cQTL) for each phenotype, resulting in a set of cQTL linked to the trait
706
Obtain abundance data for a plurality of cellular constituents from one or more tissues in each member of the population under study
708
Identify cellular constituents (association set D) whose abundance levels accross the population significantly associate with the trait of interest (e.g., by use of Pearson correlations, basic discriminant analysis, regression models, etc.)
710
For each cellular constituent i in association set D, perform quantitative genetic analysis, in which abundance levels of cellular constituent i across the population serve as a quantitative trait, in order to identify eQTL for cellular constituent i
712
Remove all cellular constituents from association set D that do not have at least one eQTL that is coincident with (within a support interval of) a cQTL for the trait of interest in order to form the candidate causative cellular constituent set. Optionally, require that all coincident eQTL/cQTL pass a pleiotropy test in order to be considered coincident. Cellular constituents removed from association set D form a candidate reactive cellular constituent set
714

FIG. 7A

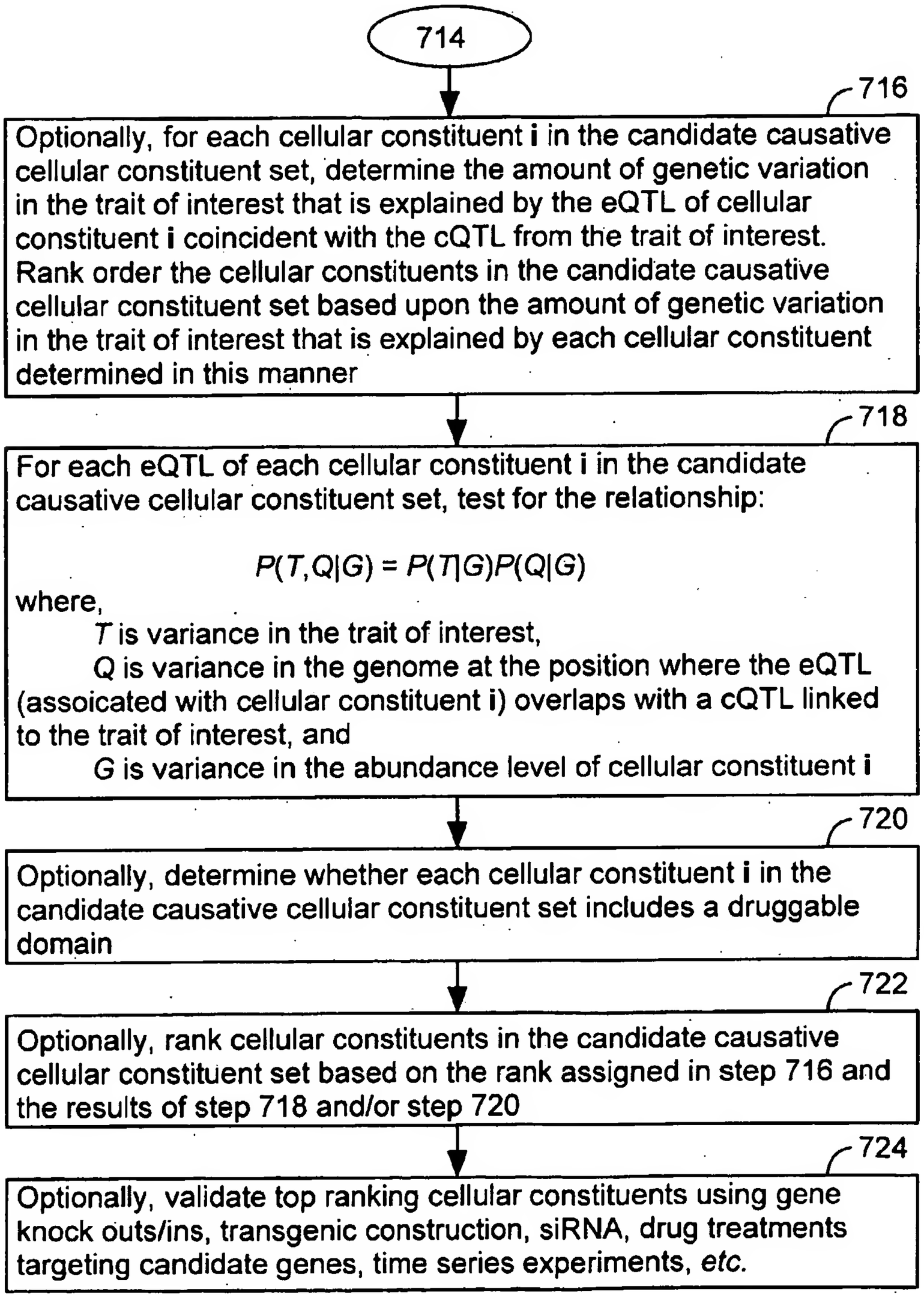

714
716
Optionally, for each cellular constituent i in the candidate causative cellular constituent set, determine the amount of genetic variation in the trait of interest that is explained by the eQTL of cellular constituent i coincident with the cQTL from the trait of interest. Rank order the cellular constituents in the candidate causative cellular constituent set based upon the amount of genetic variation in the trait of interest that is explained by each cellular constituent determined in this manner
718
For each eQTL of each cellular constituent i in the candidate causative cellular constituent set, test for the relationship:
$P(T,Q|G) = P(T|G)P(Q|G)$
where,
T is variance in the trait of interest,
Q is variance in the genome at the position where the eQTL (assoicated with cellular constituent i) overlaps with a cQTL linked to the trait of interest, and
G is variance in the abundance level of cellular constituent i
720
Optionally, determine whether each cellular constituent i in the candidate causative cellular constituent set includes a druggable domain
722
Optionally, rank cellular constituents in the candidate causative cellular constituent set based on the rank assigned in step 716 and the results of step 718 and/or step 720
724
Optionally, validate top ranking cellular constituents using gene knock outs/ins, transgenic construction, siRNA, drug treatments targeting candidate genes, time series experiments, etc.

FIG. 7B

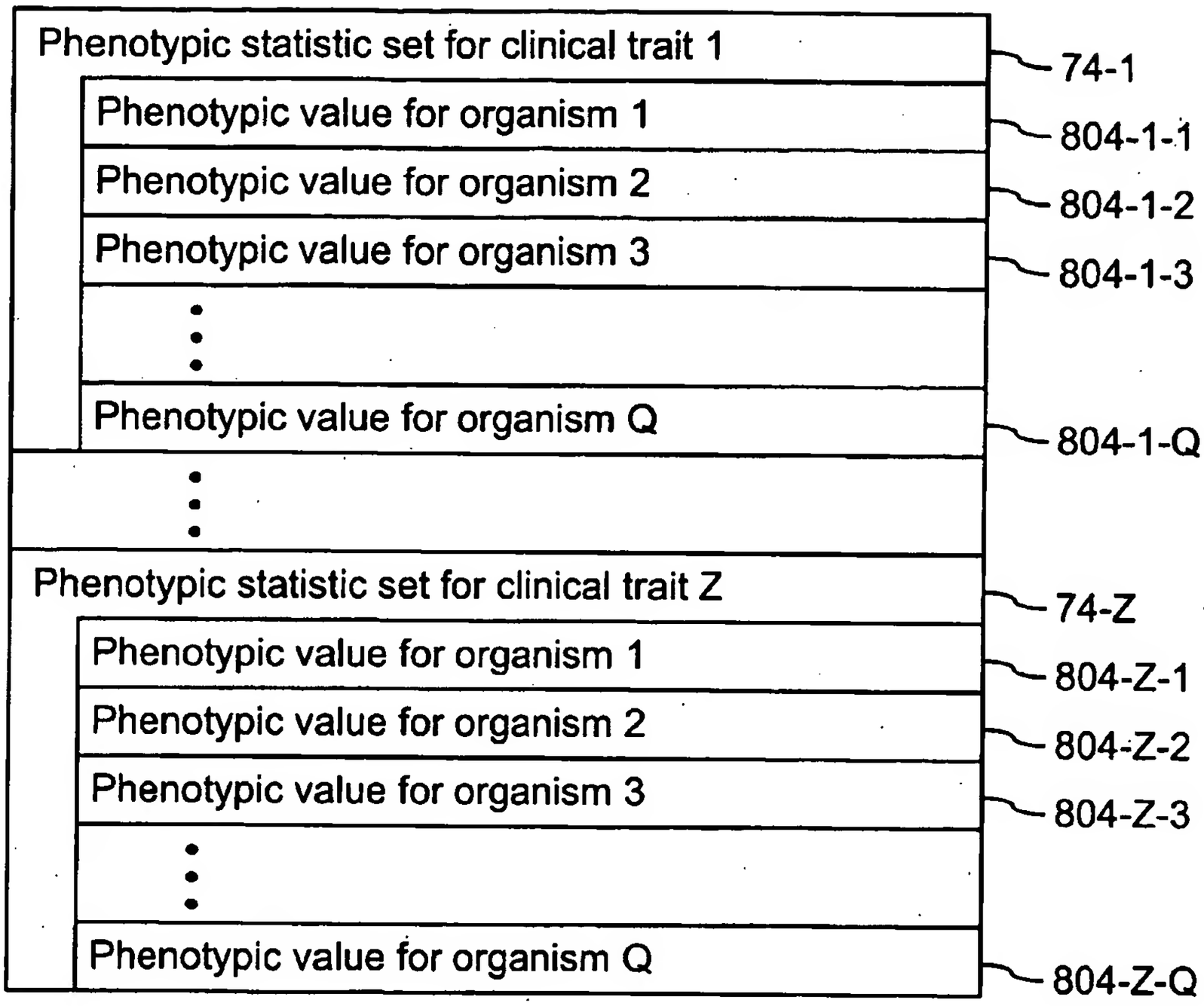

Phenotypic statistic set for clinical trait 1
74-1
Phenotypic value for organism 1
804-1-1
Phenotypic value for organism 2
804-1-2
Phenotypic value for organism 3
804-1-3
Phenotypic value for organism Q
804-1-Q
Phenotypic statistic set for clinical trait Z
74-Z
Phenotypic value for organism 1
804-Z-1
Phenotypic value for organism 2
804-Z-2
Phenotypic value for organism 3
804-Z-3
Phenotypic value for organism Q
804-Z-Q

FIG. 8

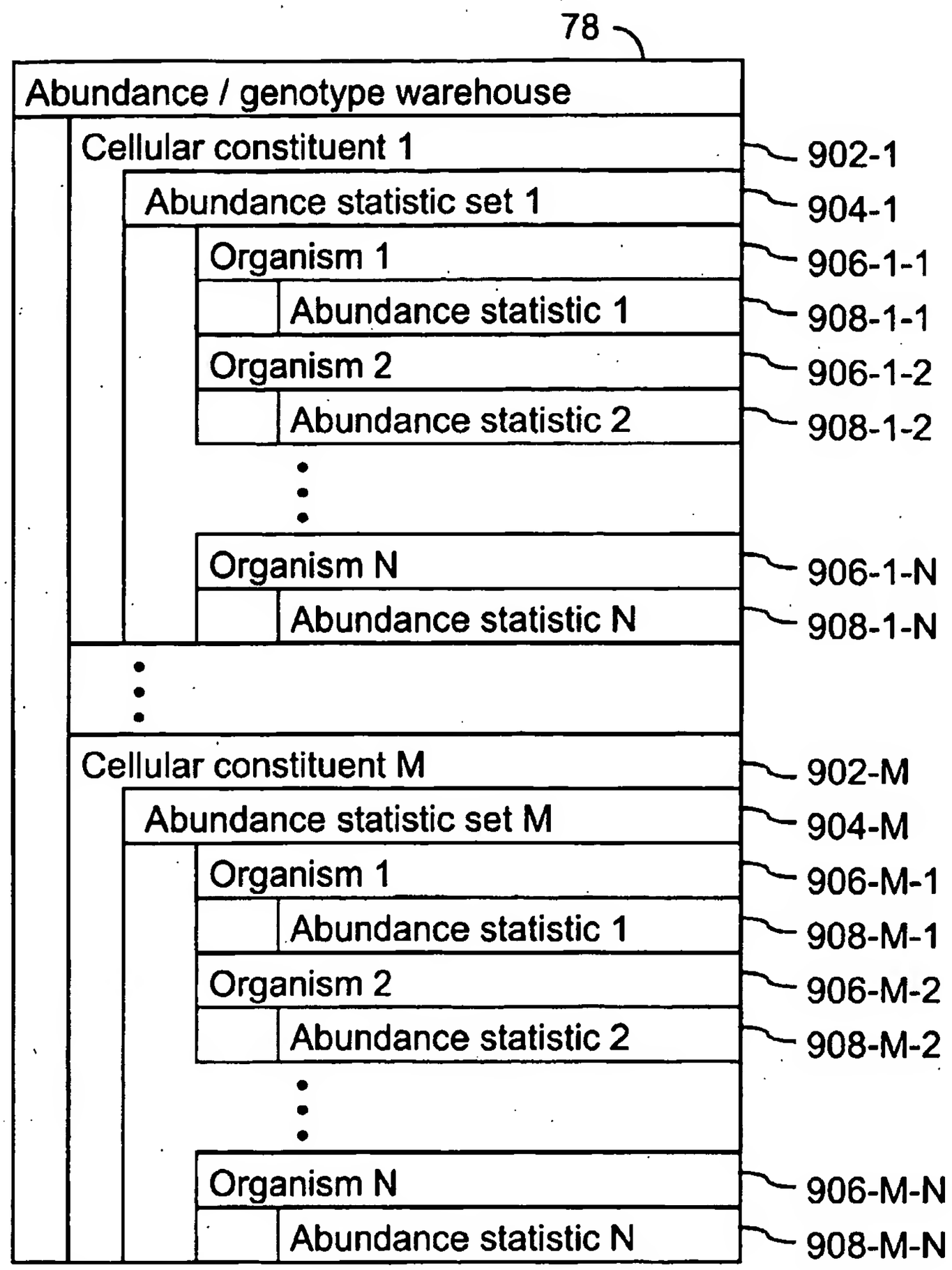

78
Abundance / genotype warehouse
Cellular constituent 1
902-1
Abundance statistic set 1
904-1
Organism 1
906-1-1
Abundance statistic 1
908-1-1
Organism 2
906-1-2
Abundance statistic 2
908-1-2
Organism N
906-1-N
Abundance statistic N
908-1-N
Cellular constituent M
902-M
Abundance statistic set M
904-M
Organism 1
906-M-1
Abundance statistic 1
908-M-1
Organism 2
906-M-2
Abundance statistic 2
908-M-2
Organism N
906-M-N
Abundance statistic N
908-M-N

FIG. 9

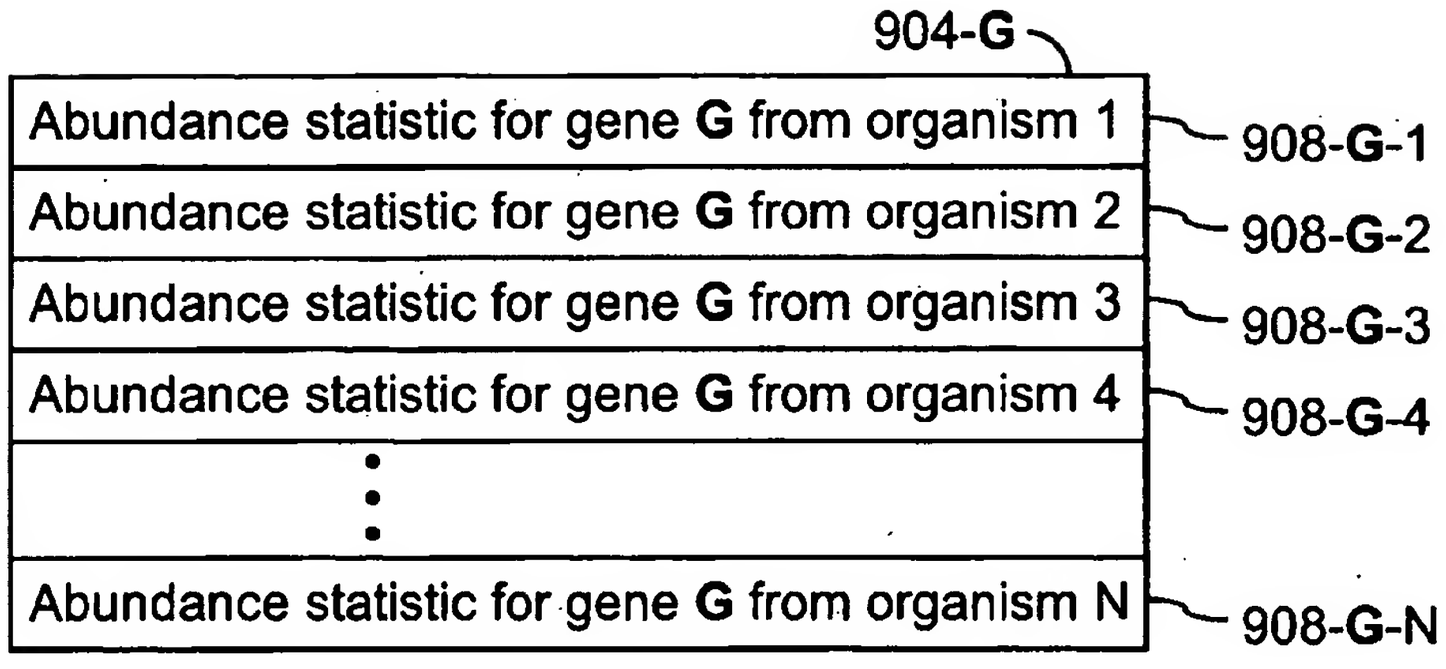

904-G
Abundance statistic for gene G from organism 1
Abundance statistic for gene G from organism 2
Abundance statistic for gene G from organism 3
Abundance statistic for gene G from organism 4
Abundance statistic for gene G from organism N
908-G-1
908-G-2
908-G-3
908-G-4
908-G-N

FIG. 10

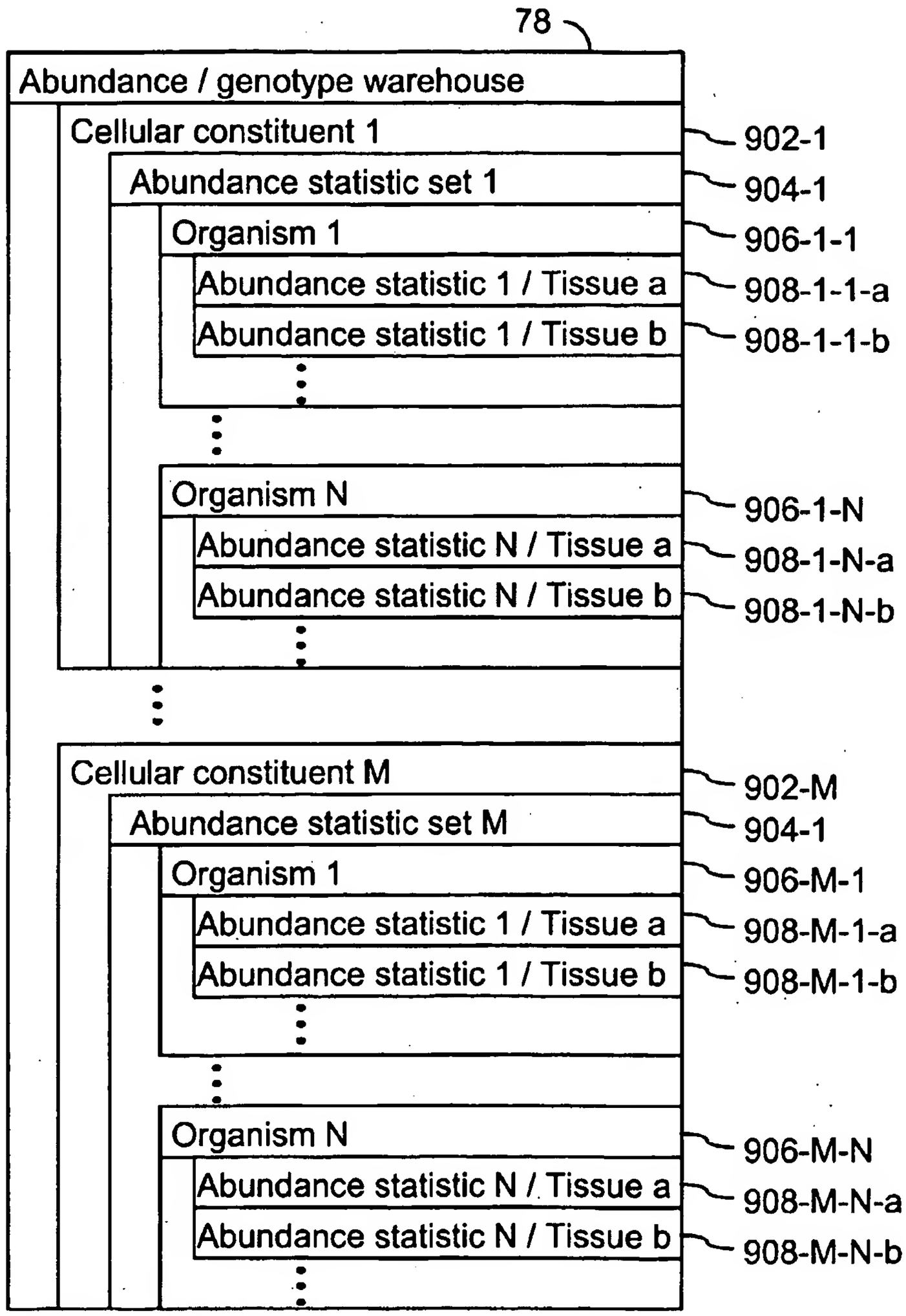

78
Abundance / genotype warehouse
Cellular constituent 1
902-1
Abundance statistic set 1
904-1
Organism 1
906-1-1
Abundance statistic 1 / Tissue a
908-1-1-a
Abundance statistic 1 / Tissue b
908-1-1-b
Organism N
906-1-N
Abundance statistic N / Tissue a
908-1-N-a
Abundance statistic N / Tissue b
908-1-N-b
Cellular constituent M
902-M
Abundance statistic set M
904-1
Organism 1
906-M-1
Abundance statistic 1 / Tissue a
908-M-1-a
Abundance statistic 1 / Tissue b
908-M-1-b
Organism N
906-M-N
Abundance statistic N / Tissue a
908-M-N-a
Abundance statistic N / Tissue b
908-M-N-b

FIG. 11

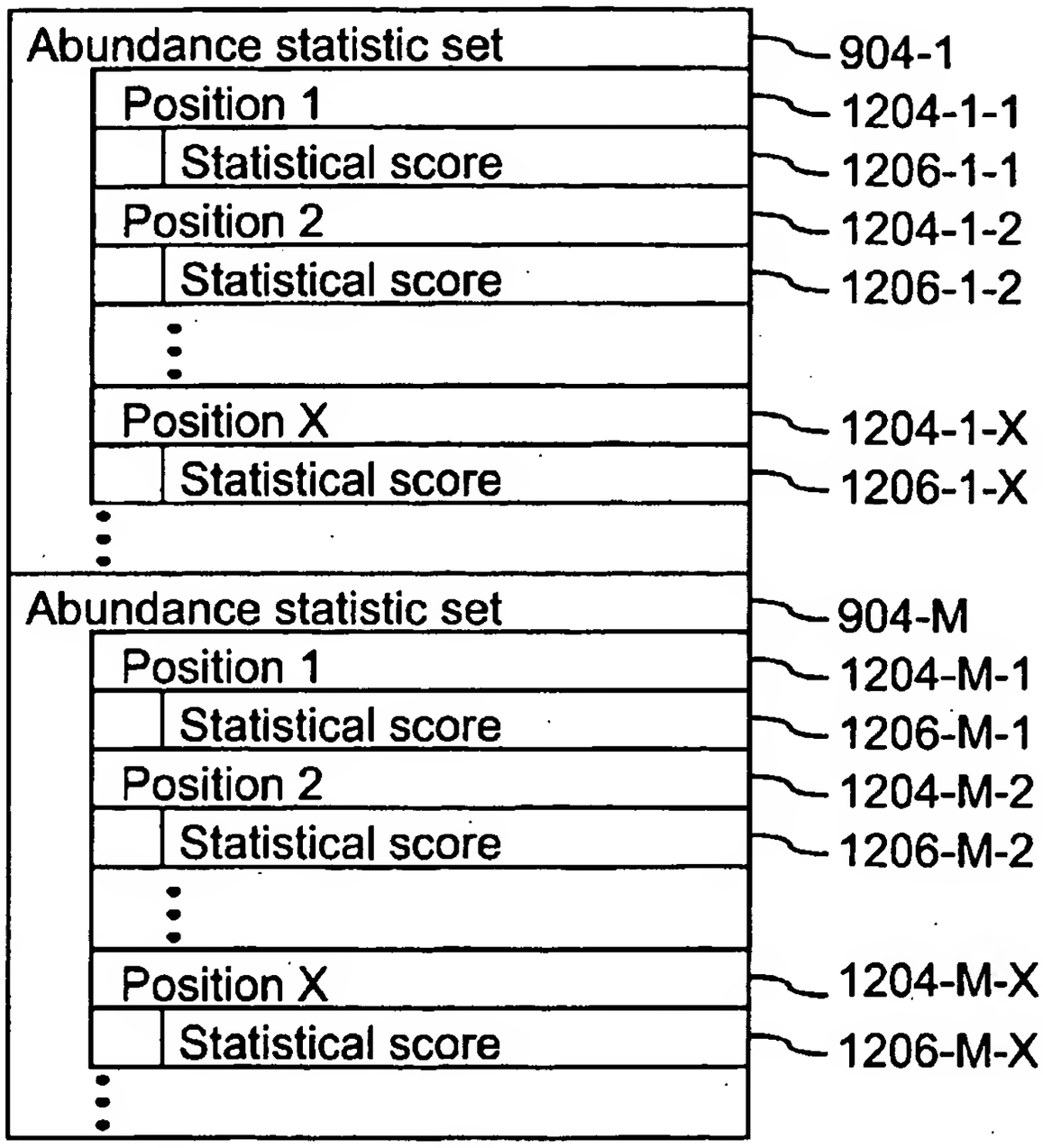

Abundance statistic set
904-1
Position 1
1204-1-1
Statistical score
1206-1-1
Position 2
1204-1-2
Statistical score
1206-1-2
Position X
1204-1-X
Statistical score
1206-1-X
Abundance statistic set
904-M
Position 1
1204-M-1
Statistical score
1206-M-1
Position 2
1204-M-2
Statistical score
1206-M-2
Position X
1204-M-X
Statistical score
1206-M-X

FIG. 12

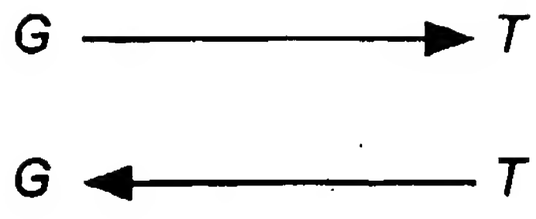


FIG. 13A

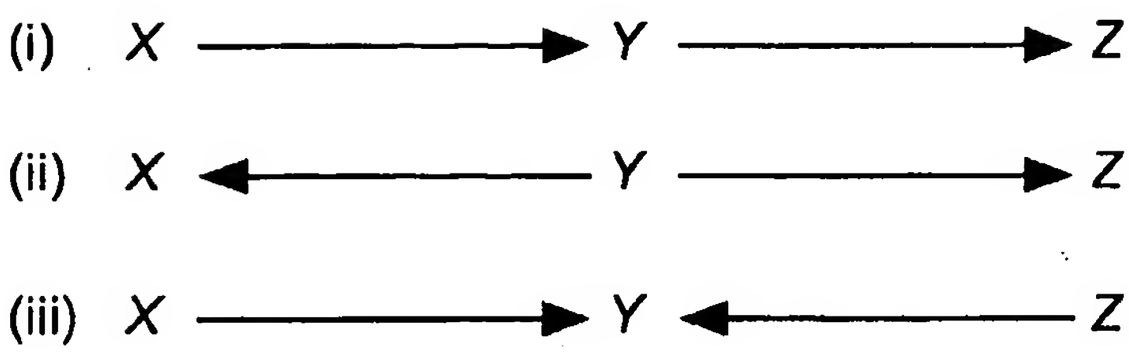


FIG. 13B

FIG. 13C

FIG. 13D

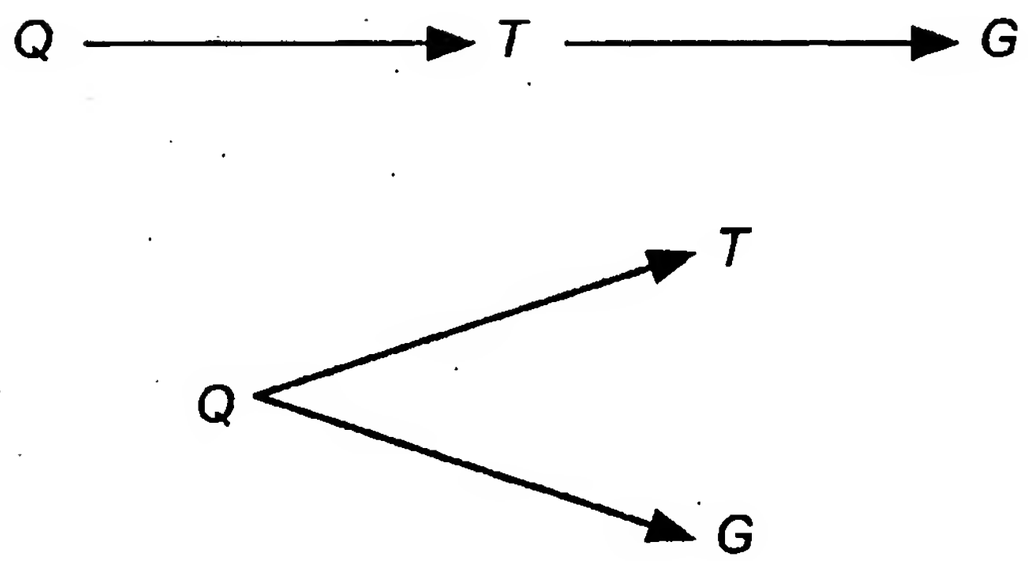


FIG. 13E

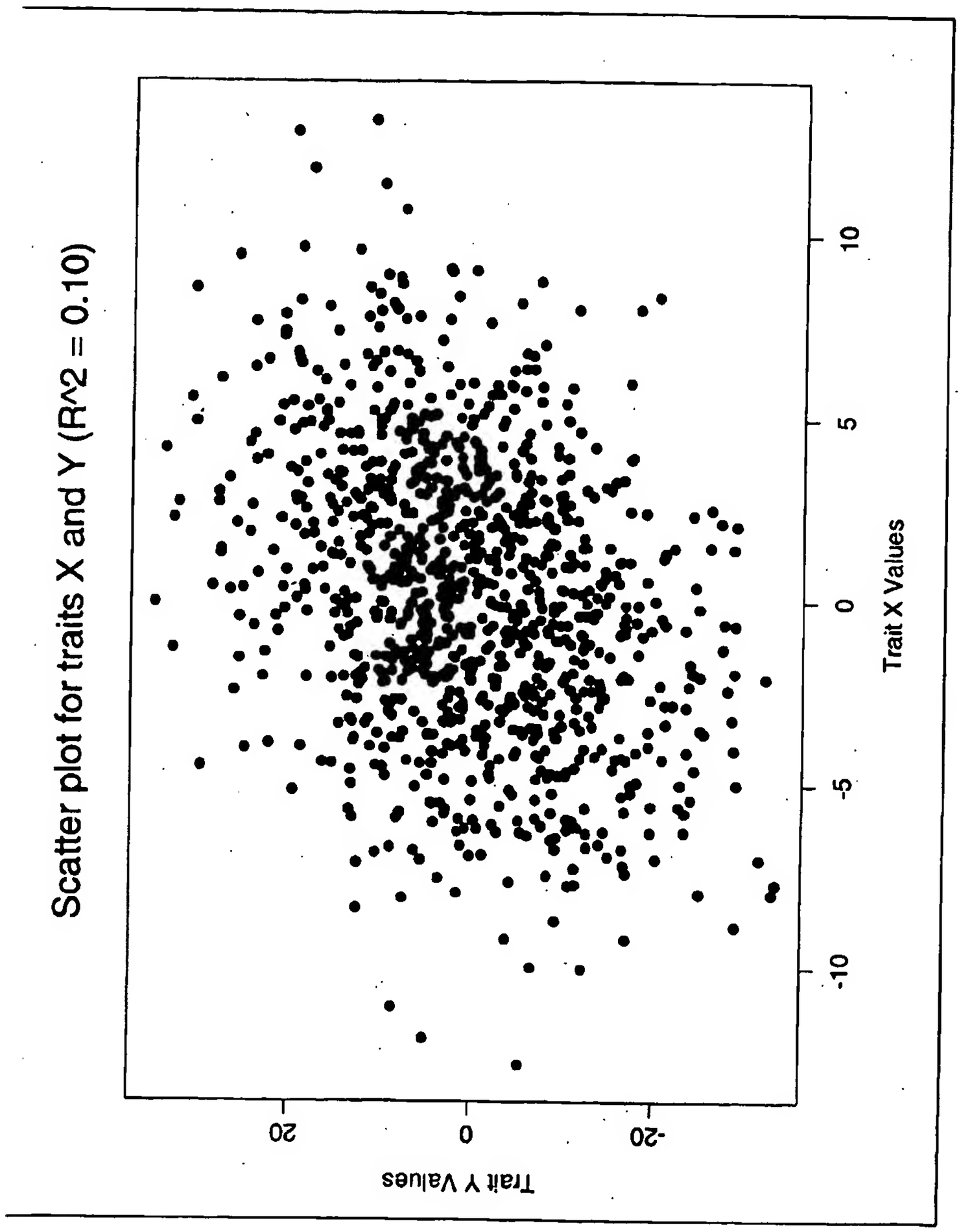

Scatter plot for traits X and Y (R^2 = 0.10)
Trait X Values
Trait Y Values
10
5
0
-5
-10
20
0
-20

Fig. 14

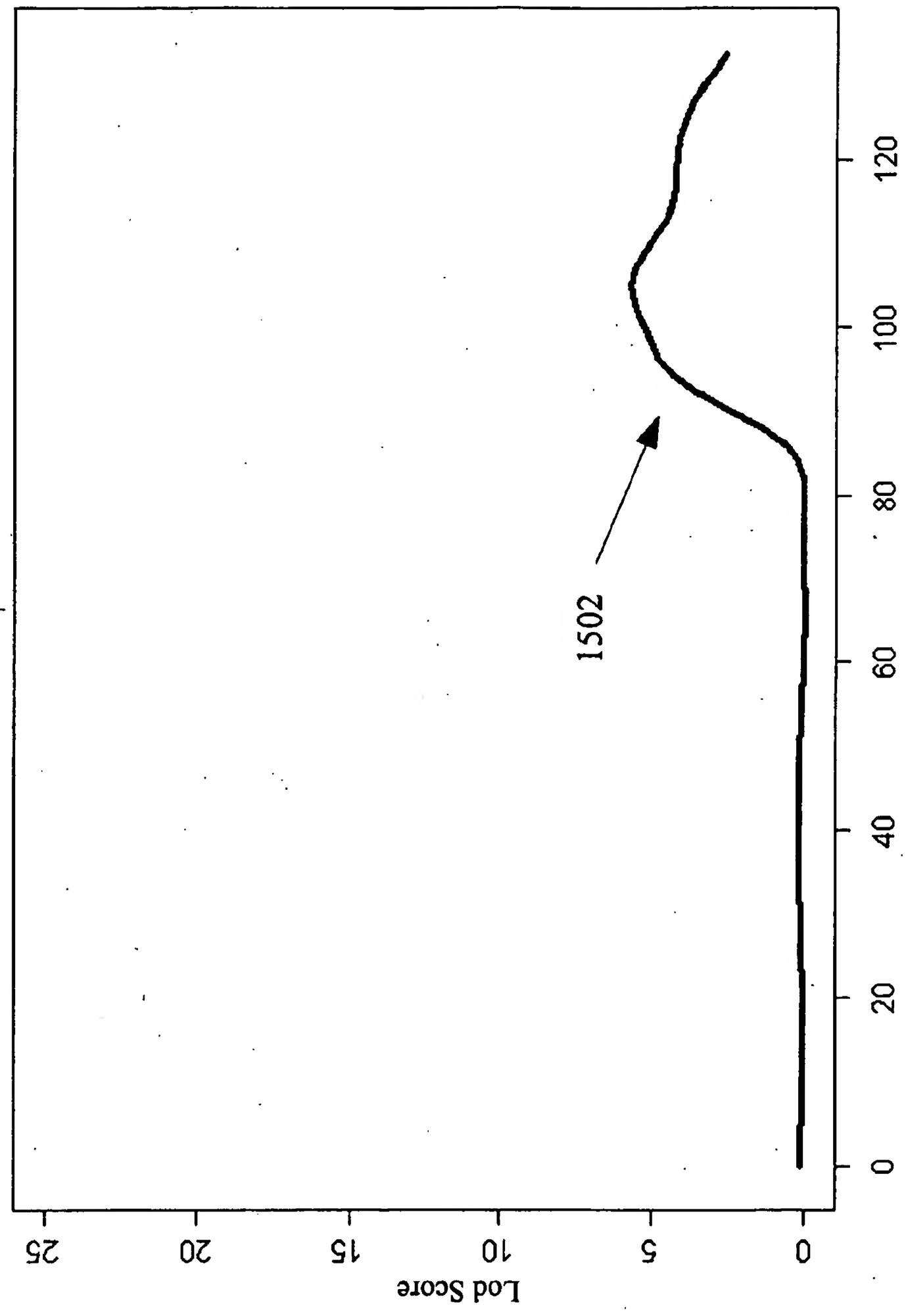

Lod Score
0
5
10
15
20
25
Chromosome 2 (cM)
0
20
40
60
80
100
120
1502

Fig. 15A

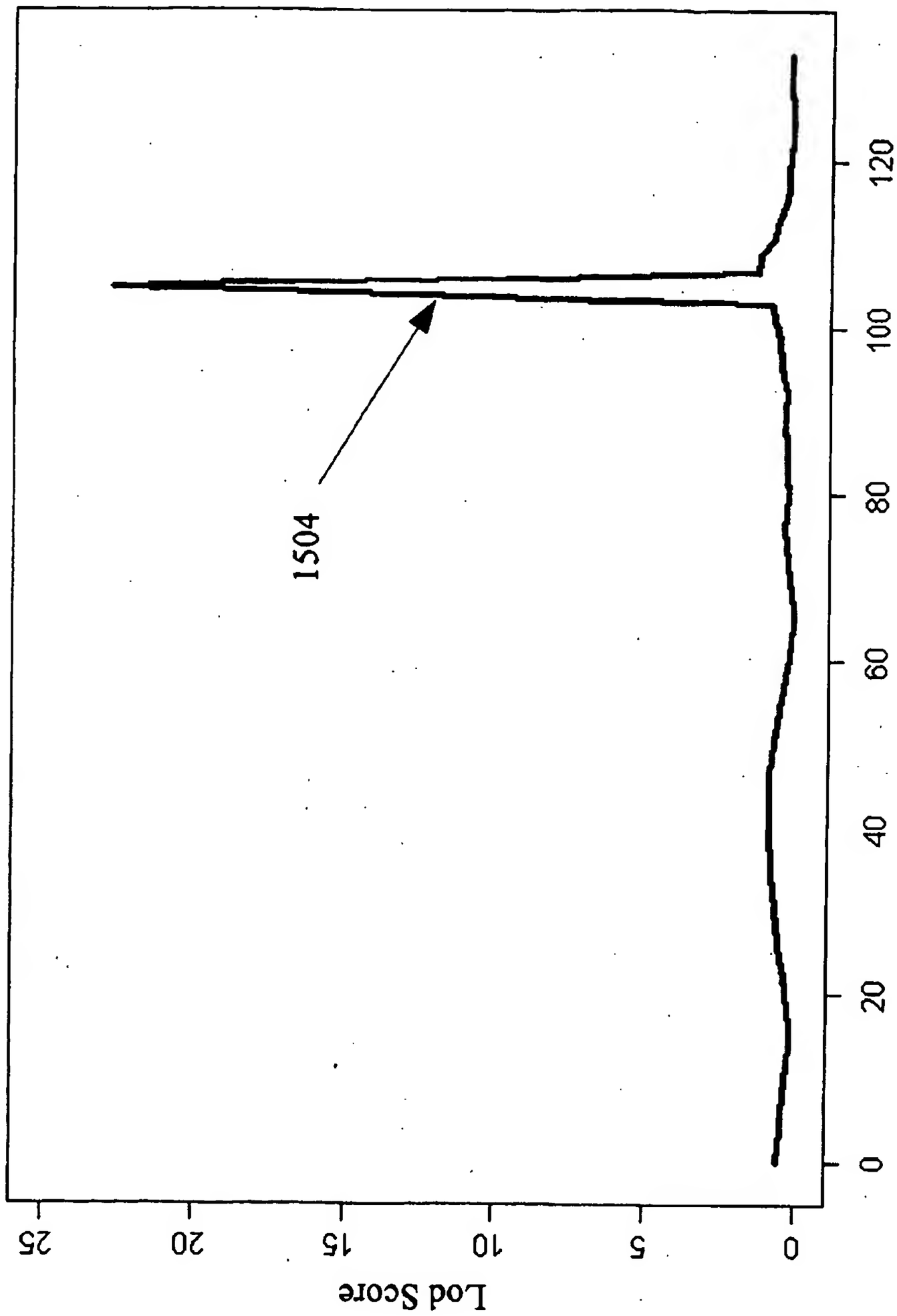

1504
Lod Score
0
5
10
15
20
25
Chromosome 2 (cM)
0
20
40
60
80
100
120

Fig. 15B

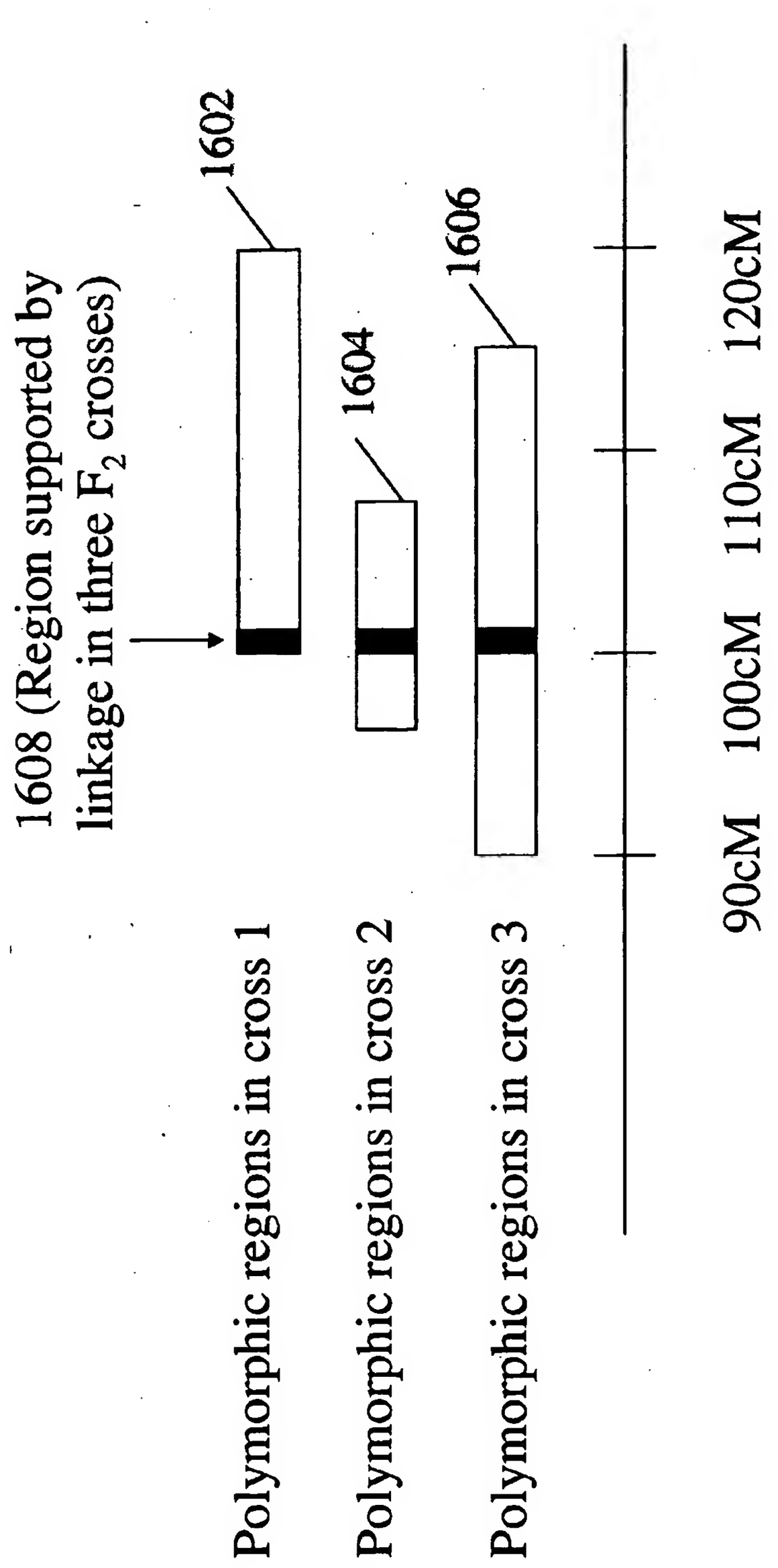

Polymorphic regions in cross 1
Polymorphic regions in cross 2
Polymorphic regions in cross 3
1608 (Region supported by linkage in three F_2 crosses)
1602
1604
1606
90cM
100cM
110cM
120cM

Fig. 16

```
          10         20         30         40         50         60
           |          |          |          |          |          |
MEPEAPRRRH THQRGYLLTR NPHLNKDLAF TLEERQQLNI HGLLPPSFNS QEIQVLRVVK

          70         80         90        100        110        120
           |          |          |          |          |          |
NFEHLNSDFD RYLLLMDLQD RNEKLFYRVL TSDIEKFMPI VYTPTVGLAC QQYSLVFRKP

         130        140        150        160        170        180
           |          |          |          |          |          |
RGLFITIHDR GHIASVLNAW PEDVIKAIVV TDGERILGLG DLGCNGMGIP VGKLALYTAC

         190        200        210        220        230        240
           |          |          |          |          |          |
GGMNPQECLP VILDVGTENE ELLKDPLYIG LRQRRVRGSE YDDFLDEFME AVSSKYGMNC

         250        260        270        280        290        300
           |          |          |          |          |          |
LIQFEDFANV NAFRLLNKYR NQYCTFNDDI QGTASVAVAG LLAALRITKN KLSDQTILFQ

         310        320        330        340        350        360
           |          |          |          |          |          |
GAGEAALGIA HLIVMALEKE GLPKEKAIKK IWLVDSKGLI VKGRASLTQE KEKFAHEHEE

         370        380        390        400        410        420
           |          |          |          |          |          |
MKNLEAIVQE IKPTALIGVA AIGGAFSEQI LKDMAAFNER PIIFALSNPT SKAECSAEQC

         430        440        450        460        470        480
           |          |          |          |          |          |
YKITKGRAIF ASGSPFDPVT LPNGQTLYPG QGNNSYVFPG VALGVVACGL RQITDNIFLT

         490        500        510        520        530        540
           |          |          |          |          |          |
TAEVIAQQVS DKHLEEGRLY PPLNTIRDVS LKIAEKIVKD AYQEKTATVY PEPQNKEAFV

         550        560        570
           |          |          |
RSQMYSTDYD QILPDCYSWP EEVQKIQTKV DQ
```

(SEQ ID NO: 1)

Fig. 17

```
        10          20          30          40          50          60
        |           |           |           |           |           |
MEPRAPRRRH THQRGYLLTR DPHLNKDLAF TLEERQQLNI HGLLPPCIIS QELQVLRIIK

        70          80          90          100         110         120
        |           |           |           |           |           |
NFERLNSDFD RYLLLMDLQD RNEKLFYSVL MSDVEKFMPI VYTPTVGLAC QQYSLAFRKP

        130         140         150         160         170         180
        |           |           |           |           |           |
RGLFISIHDK GHIASVLNAW PEDVVKAIVV TDGERILGLG DLGCNGMGIP VGKLALYTAC

        190         200         210         220         230         240
        |           |           |           |           |           |
GGVNPQQCLP ITLDVGTENE ELLKDPLYIG LRHRRVRGPE YDAFLDEFME AASSKYGMNC

        250         260         270         280         290         300
        |           |           |           |           |           |
LIQFEDFANR NAFRLLNKYR NKYCTFNDDI QGTASVAVAG LLAALRITKN KLSDQTVLFQ

        310         320         330         340         350         360
        |           |           |           |           |           |
GAGEAALGIA HLVVMAMEKE GLSKENARKK IWLVDSKGLI VKGRASLTEE KEVFAHEHEE

        370         380         390         400         410         420
        |           |           |           |           |           |
MKNLEAIVQK IKPTALIGVA AIGGAFTEQI LKDMAAFNER PIIFALSSPT SKAECSADEC

        430         440         450         460         470         480
        |           |           |           |           |           |
YKVTKGRAIF ASGSPFDPVT LPDGRTLFPG QGNNSYVFPG VALGVVACGL RHIDDKVFLT

        490         500         510         520         530         540
        |           |           |           |           |           |
TREVISQQVS DKHLQEGRLY PPLNTIRGVS LKIAVKIVQD AYKEKMATVY PEPQNKEEFV

        550         560         570
        |           |           |
SSQMYSTNYD QILPDCYPWP AEVQKIQTKV NQ
```

(SEQ ID NO: 2)

Fig. 18

Chr	Pos (M)	LOD
1	1.12	1.62
3	0.92	1.59
5	0.00	1.93
6	0.47	2.84
9	0.08	2.53
19	0.18	1.60

Chr	Pos (M)	LOD
6	0.42	4.45
9	0.10	5.56
13	1.02	3.91
16	0.00	3.16
17	0.57	2.17
19	0.22	2.00

Fig. 19A

Trait	No. of overlaps with Mod1
sqrtretrog	2
fatbw	1
livebwt	1
omen	1
subc	1
ins	0
retrog	0

Trait	No. of overlaps with Mod1
logomen	3
epipa	2
ftpsum	2
lep	2
logftpsum	2
logsubc	2
sqrtepipa	2
sqrtlep	2

Fig. 19B

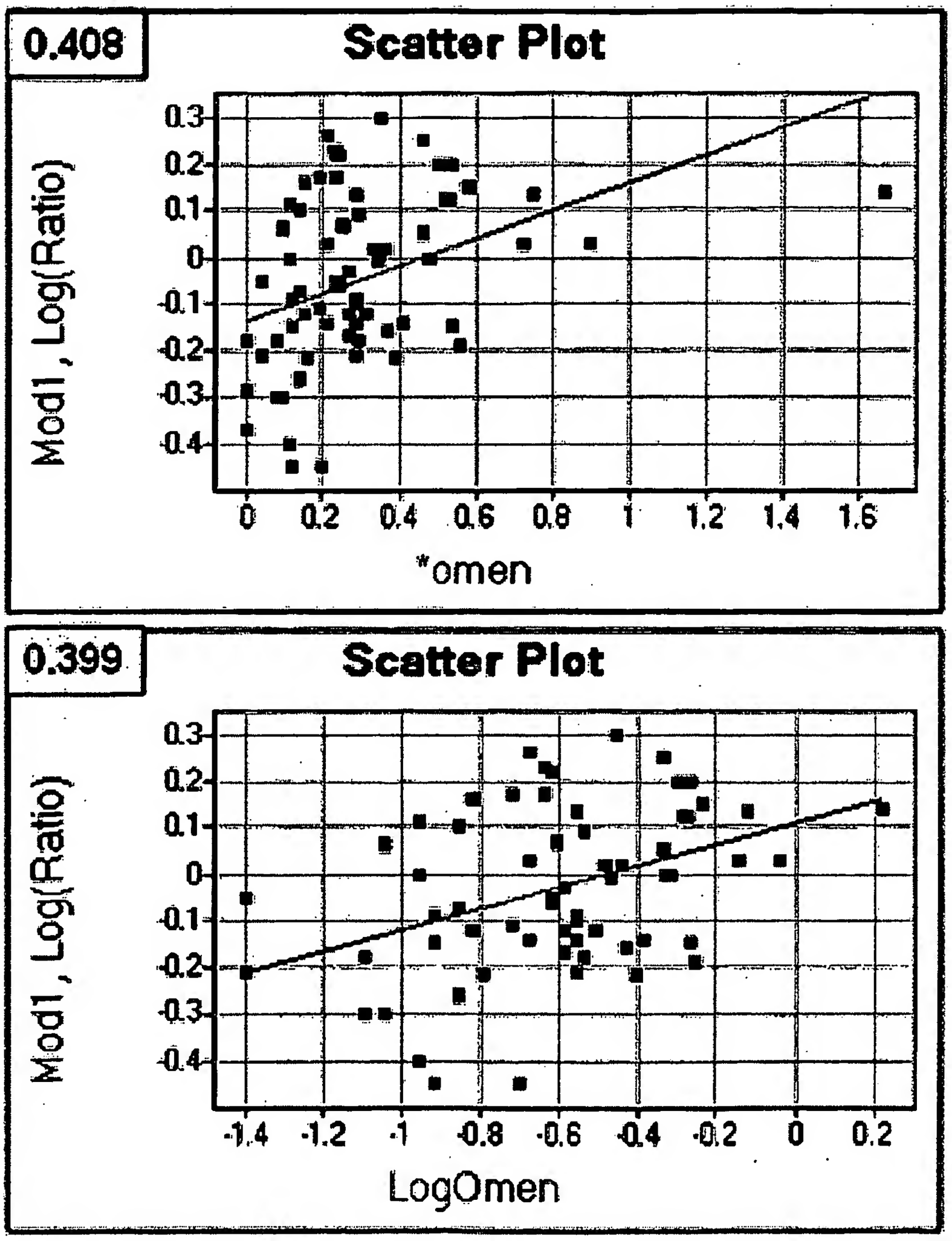

0.408
Scatter Plot
Mod1, Log(Ratio)
0.3
0.2
0.1
0
-0.1
-0.2
-0.3
-0.4
0
0.2
0.4
0.6
0.8
1
1.2
1.4
1.6
*omen
0.399
Scatter Plot
Mod1, Log(Ratio)
0.3
0.2
0.1
0
-0.1
-0.2
-0.3
-0.4
-1.4
-1.2
-1
-0.8
-0.6
-0.4
-0.2
0
0.2
LogOmen

Fig. 20

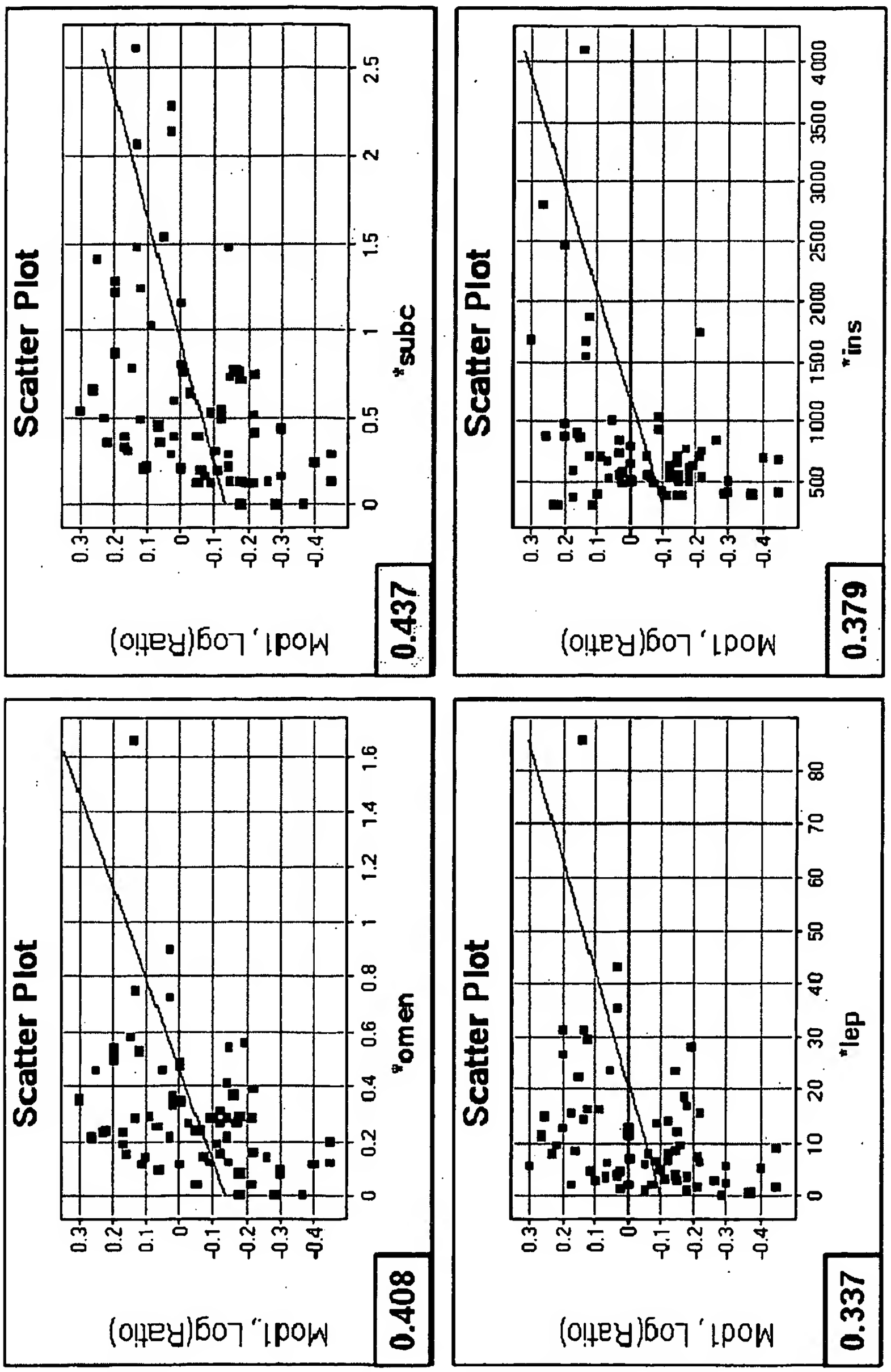

Scatter Plot
Mod1, Log(Ratio)
0.437
*subc
Scatter Plot
Mod1, Log(Ratio)
0.379
*ins
Scatter Plot
Mod1, Log(Ratio)
0.408
*omen
Scatter Plot
Mod1, Log(Ratio)
0.337
*lep

Figure 21

	*livebwt	*retrog	*epipa	*omen	*subc	*ftpsum	*fatbw	*lep	Mod1
*livebwt	1								
*retrog									
*epipa									
*omen									
*subc									
*ftpsum									
*fatbw									
*lep									
Mod1									

	*livebwt	*retrog	*epipa	*omen	*subc	*ftpsum	*fatbw	*lep	Mod1
*livebwt	1	0.56	0.65	0.64	0.62	0.67	0.43	0.67	0.23
*retrog		1	0.77	0.78	0.75	0.82	0.78	0.76	0.49
*epipa			1	0.89	0.86	0.99	0.91	0.94	0.36
*omen				1	0.84	0.92	0.82	0.92	0.41
*subc					1	0.92	0.87	0.85	0.44
*ftpsum						1	0.92	0.95	0.41
*fatbw							1	0.82	0.45
*lep								1	0.34
Mod1									1

Figure 22

```
  1  IKEKGKPLXL NPRTNKGXAF TLQERQXLGL QGLLPPKIET QDIQALRFHR
 51  NLKKXTSPLE KYIYIXGIQE RNEKLFYRIL QDDIESLXPI VYTPTVGLAC
101  SQYGHIFRRP KGLFISISDR GHVRSIVDNW PENHVKAVVV TDGERILGLG
151  DLGVYGXGIP VGKLCLYTAC AGIRPDRCLP VCIDVGTDNI ALLKDPFYXG
201  LYQKRDRTQQ YDDLIDEFXK AITDRYGRNT LIQFEDFGNH NAFRFLRKYR
251  EKYCTFNDDI QGTAAVALAG LLAAQKVISK PISEHKILFL GAGEAALGIA
301  NLIVXSXVEN GLSEQEAQKK IWXFDKYGLL VKGRKAKIDS YQEPFTHSAP
351  ESIPDTFEDA VNILKPSTII GVAGAGRLFT PDVIRAXASI NERPVIFALS
401  NPTAQAECTA EEAYTLTEGR CLFASGSPFG PVKLTDGRVF TPGQGNNVYI
451  FPGVALAVIL CNTRHISDSV FLEAAKALTS QLTDEELAQG RLYPPLANIQ
501  EVSINIAIKV TEYLYANKXA FRYPEPEDKA KYVKERTWRS EYDSLLPDVY
551  EWPESASSPP VITE
```

(SEQ ID NO: 3)

Fig. 23

```
        10         20         30         40         50         60
         |          |          |          |          |          |
MLSRLRVVST TCTLACRHLH IKEKGKPLML NPRTNKGMAF TLQERQMLGL QGLLPPKIET

        70         80         90        100        110        120
         |          |          |          |          |          |
QDIQALRFHR NLKKMTSPLE KYIYIMGIQE RNEKLFYRIL QDDIESLMPI VYTPTVGLAC

       130        140        150        160        170        180
         |          |          |          |          |          |
SQYGHIFRRP KGLFISISDR GHVRSIVDNW PENHVKAVVV TDGERILGLG DLGVYGMGIP

       190        200        210        220        230        240
         |          |          |          |          |          |
VGKLCLYTAC AGIRPDRCLP VCIDVGTDNI ALLKDPFYMG LYQKRDRTQQ YDDLIDEFMK

       250        260        270        280        290        300
         |          |          |          |          |          |
AITDRYGRNT LIQFEDFGNH NAFRFLRKYR EKYCTFNDDI QGTAAVALAG LLAAQKVISK

       310        320        330        340        350        360
         |          |          |          |          |          |
PISEHKILFL GAGEAALGIA NLIVMSMVEN GLSEQEAQKK IWMFDKYGLL VKGRKAKIDS

       370        380        390        400        410        420
         |          |          |          |          |          |
YQEPFTHSAP ESIPDTFEDA VNILKPSTII GVAGAGRLFT PDVIRAMASI NERPVIFALS

       430        440        450        460        470        480
         |          |          |          |          |          |
NPTAQAECTA EEAYTLTEGR CLFASGSPFG PVKLTDGRVF TPGQGNNVYI FPGVALAVIL

       490        500        510        520        530        540
         |          |          |          |          |          |
CNTRHISDSV FLEAAKALTS QLTDEELAQG RLYPPLANIQ EVSINIAIKV TEYLYANKMA

       550        560        570        580
         |          |          |          |
FRYPEPEDKA KYVKERTWRS EYDSLLPDVY EWPESASSPP VITE
```

(SEQ ID NO: 4)

Fig. 24

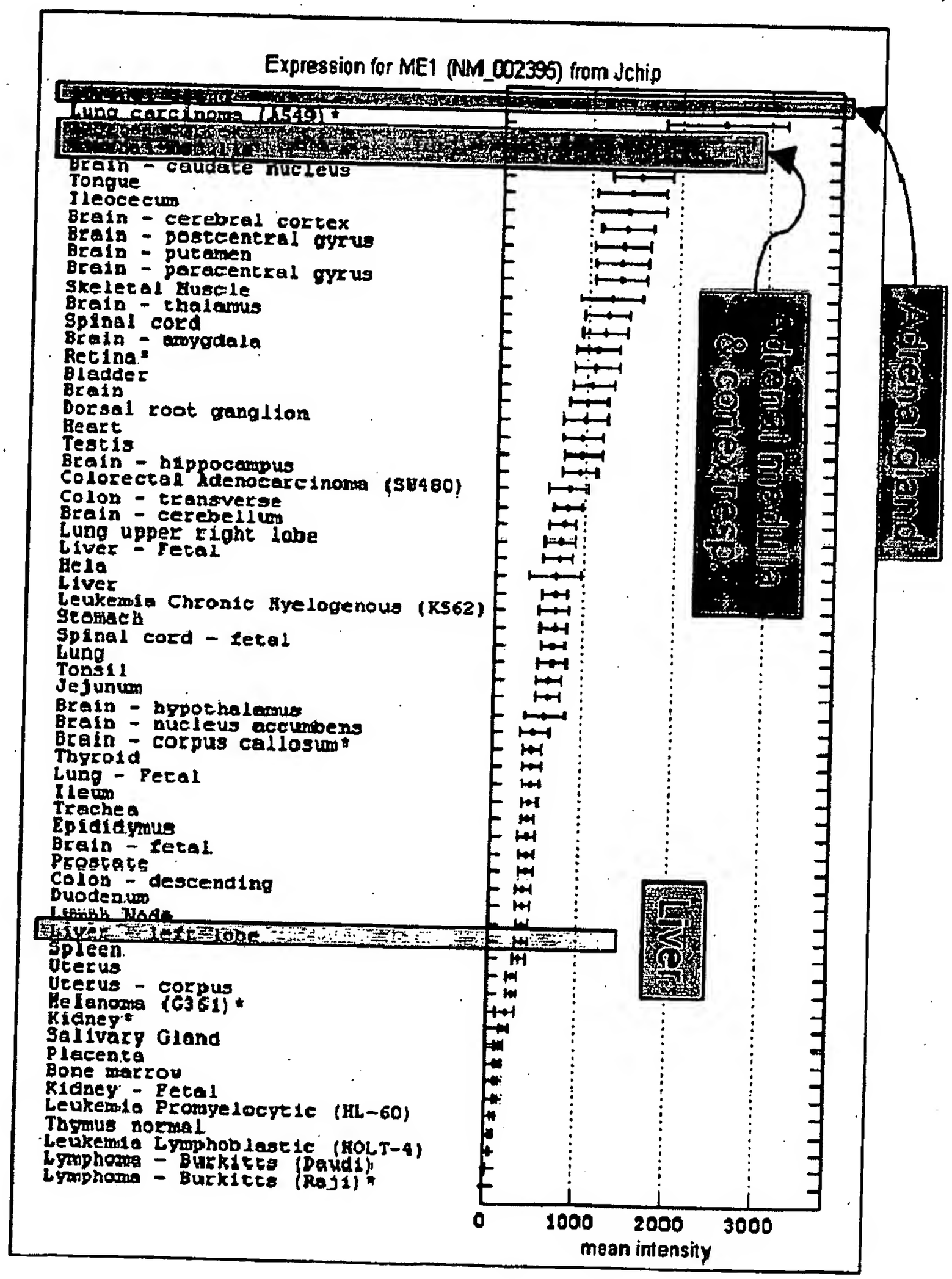

Expression for ME1 (NM_002395) from Jchip
Lung carcinoma (A549)*
Brain - caudate nucleus
Tongue
Ileocecum
Brain - cerebral cortex
Brain - postcentral gyrus
Brain - putamen
Brain - paracentral gyrus
Skeletal Muscle
Brain - thalamus
Spinal cord
Brain - amygdala
Retina*
Bladder
Brain
Dorsal root ganglion
Heart
Testis
Brain - hippocampus
Colorectal Adenocarcinoma (SW480)
Colon - transverse
Brain - cerebellum
Lung upper right lobe
Liver - Fetal
Hela
Liver
Leukemia Chronic Myelogenous (K562)
Stomach
Spinal cord - fetal
Lung
Tonsil
Jejunum
Brain - hypothalamus
Brain - nucleus accumbens
Brain - corpus callosum*
Thyroid
Lung - Fetal
Ileum
Trachea
Epididymus
Brain - fetal
Prostate
Colon - descending
Duodenum
Lymph Node
Liver - left lobe
Spleen
Uterus
Uterus - corpus
Melanoma (G361)*
Kidney*
Salivary Gland
Placenta
Bone marrow
Kidney - Fetal
Leukemia Promyelocytic (HL-60)
Thymus normal
Leukemia Lymphoblastic (NOLT-4)
Lymphoma - Burkitts (Daudi)
Lymphoma - Burkitts (Raji)*
Adrenal gland
Pituitary gland & Adrenal medulla
Liver
0
1000
2000
3000
mean intensity

Fig. 25

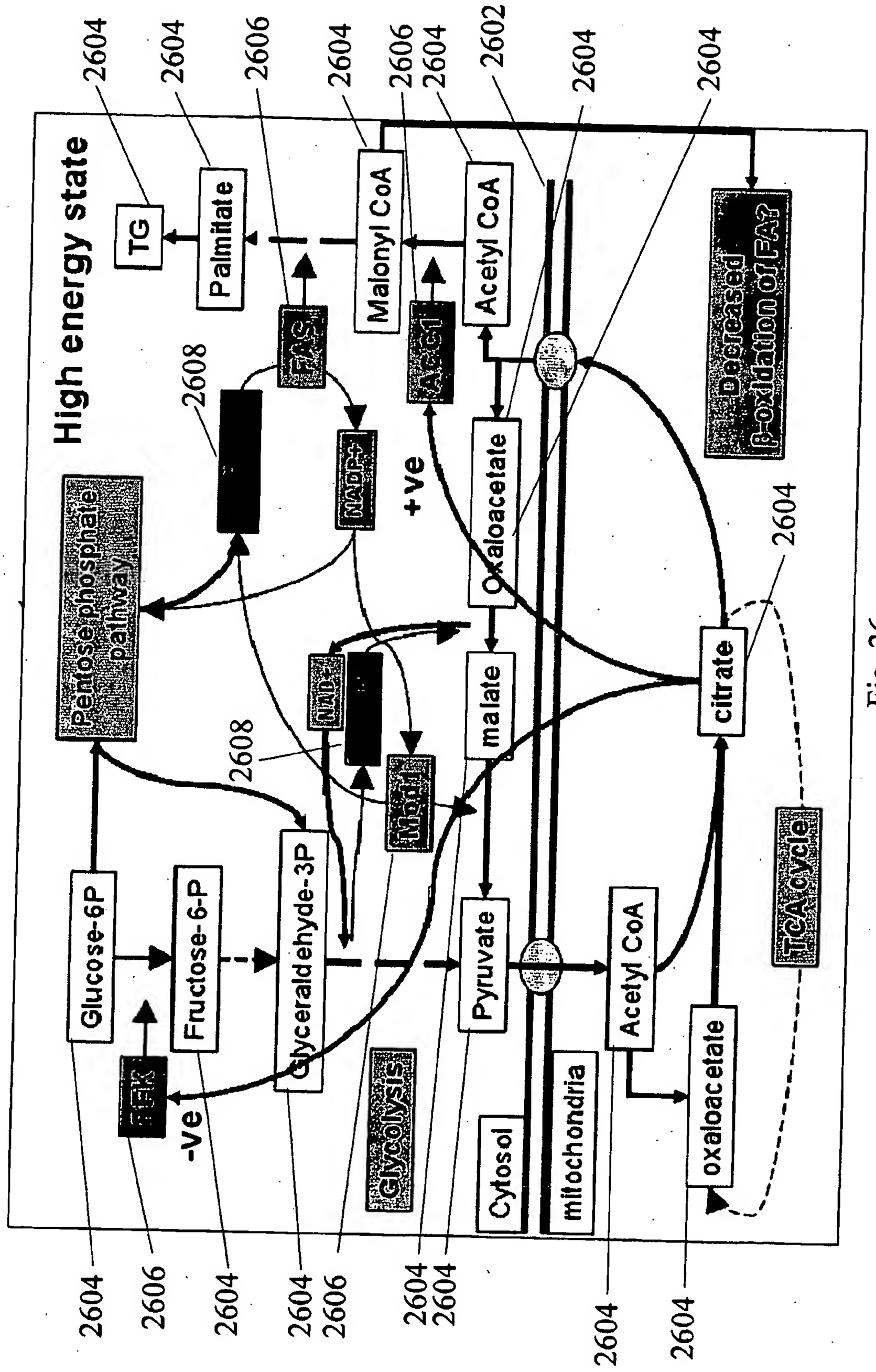

High energy state
TG
Palmitate
FAS
Malonyl CoA
ACC1
Acetyl CoA
Decreased β-oxidation of FA?
2608
NADPH
+ve
Pentose phosphate pathway
Glucose-6P
Fructose-6-P
Glyceraldehyde-3P
NADH
Mdh1
malate
Oxaloacetate
citrate
TCA Cycle
FBP1
-ve
Glycolysis
Pyruvate
Cytosol
mitochondria
Acetyl CoA
oxaloacetate
2604
2606
2602
2608

Fig. 26

```
   1 atggccttta cccttgaaga aaggctgcag cttggaatcc acggcctaat cccgccctgc
  61 tttctgagcc aggacgtcca gctcctccga atcatgagat attacgagcg gcagcagagt
 121 gacctggaca agtacatcat tctcatgaca ctccaagacc gtaacgagaa gctcttctac
 181 cgagtgctga cttcggacgt ggagaagttc atgccaatcg tgtacacgcc taccgtgggg
 241 ctagcctgtc agcactatgg cctgactttc cgcaggcccc gtggactgtt catcaccatt
 301 catgacaaag gtcatcttgc aacaatgctg aattcttggc cagaagacaa tattaaggcc
 361 gtggtggtga ctgatgggga gcgcatcctg ggcctgggag acctgggctg ctacggcatg
 421 ggcatccctg tgggcaagct ggccctgtac acggcatgcg gaggggtgaa cccgcagcag
 481 tgcctccctg tgctgctgga cgtcggcacc aacaatgagg agctgctcag agaccctctg
 541 tacatcggcc tgaaacacca gcgcgtgcac gggaaggcat acgatgactt gctggatgag
 601 ttcatgcagg ctgtgacaga caagtttgga ataaattgcc tcatccaatt tgaagacttc
 661 gccaatgcca atgccttccg cctgctcaac aaataccgta acaagtactg catgttcaat
 721 gatgacatcc aagatgactt ctccagaggc ccaaagaggt cacaactttt cttcaagtga
```

(SEQ ID NO: 5)

Fig. 27

```
   1 atgttgtccg ggttaagcgt agtttccacc acttgtactt tggcatgtct acatttacac
  61 ataaaagaaa aaggcaagcc acttatgctg aatccaagaa caaacaaggg aatggcattt
 121 actttacaag aacgacagat gcttggtctt caagggcttc tacctcccca aatacagaca
 181 taagatattc aagccttacg attccataga aacttgaaaa aaatgactag cccttcggaa
 241 aactatatct acataatggg aatacaagaa agaaatgata aattgtttta tagaatactg
 301 caagatgaca cggagagttt aatgccaatt gcatatacac cgacggttgg tcttgtctgc
 361 tcccagtgtg gacacctctt tagaagacct aagggattat ttatttccat ctcagacaga
 421 ggtcatgtta gatcaattgt ggataagtgg ccagaaaatc atgttaaggc tgttttagtg
 481 actgatggag agagaattct gggtcatgga gatctgggtg tctatggaat gggaattcca
 541 gtaggaaaaa tttgtttgta tacagtttgt ccaggaatat ggcctgatag atgccttctg
 601 gtgtgtattg atgtgggagc tgataatatc gcactcttaa aaggcacatt ttacatgggc
 661 ttgtaccaga aacgagatcg cacacaacag tctgatgatc caattgatga gtttatgaaa
 721 gctattactg acagatatgg ctggaacaca ctccttcagt ttgaaggttt tggacatcat
 781 aatgcattca gattcttgag aaaataccaa taaaaatgtt gcactttcaa tgatgatatt
 841 caagggacag ctgcagtagc tctaataggt cttcttgcaa cacaaaaagt tactagtaaa
 901 ccaatctccg aacacaaaat cttattcctt ggagcaggag agattactct tagaattgca
 961 aatcttgtag tattgtctat ggtagaaaat ggcctgtcag aagaagaggc acaaaagaaa
1021 atctggatgt ttgacaagta tggtttatta gtttaggggc agaaagcaaa aatagattgt
1081 tatcaggaac catttactta cccagtccca gagagcatac ctgatacttt tgaagatgca
1141 gtgaatataa tgaagacttc aactacaatt ggagttgcag gtgctggccg tcttttcact
1201 cctgatgtaa tcagagccat tggctgtatc aatgaaaggc ctgtaatatt tgcattaagt
1261 aatcctacag cacaggcgga gtgcaggagt tgcacggctg gagaagcata tacacttaca
1321 gagggcaaat gtttgtttgc cagtggcagt ccatttgggc cagtgaaact cacagatggg
1381 cgaatcttta caccagatcg aggaaacaat gtatatattt ttccaggtgt gactttagct
1441 gttattctct gtaacaccca gcaaattagt gacaatgttt tcctagaagc tgcaaaggca
1501 ttgacaagcc acgtgacgga tgacgcgcta gcccgaggga gactttactt accacttgct
1561 aatattcaga aagtttctat taacattgct attaaagtta cagaatacct gtatgctaat
1621 aaaatggctt tctcaatacc cagaacctga
```

(SEQ ID NO: 6)

Fig. 28

```
   1 ccgccgccac agctgcagtc agcaccgtca ccccagcagc atccgccgcc tgcaccgcgc
  61 gtgcggcccg ccccggcctg accccgccgc cgaacccggc gccagccatg gagcccgaag
 121 ccccccgtcg ccgccacacc catcagcgcg gctacctgct gacacggaac cctcacctca
 181 acaaggactt ggcctttacc ctggaagaga gacagcaatt gaacattcat ggattgttgc
 241 caccttcctt caacagtcag gagatccagg ttcttagagt agtaaaaaat ttcgagcatc
 301 tgaactctga ctttgacagg tatcttctct taatggatct ccaagataga aatgaaaaac
 361 tcttttatag agtgctgaca tctgacattg agaaattcat gcctattgtt tatactccca
 421 ctgtgggtct ggcttgccaa caatatagtt tggtgtttcg gaagccaaga ggtctcttta
 481 ttactatcca cgatcgaggg catattgctt cagttctcaa tgcatggcca gaagatgtca
 541 tcaaggccat tgtggtgact gatggagagc gtattcttgg cttgggagac cttggctgta
 601 atggaatggg catccctgtg ggtaaattgg ctctatatac agcttgcgga gggatgaatc
 661 ctcaagaatg tctgcctgtc attctggatg tgggaaccga aaatgaggag ttacttaaag
 721 atccactcta cattggacta cggcagagaa gagtaagagg ttctgaatat gatgatttct
 781 tggacgaatt catggaggca gtttcttcca agtatggcat gaattgcctt attcagtttg
 841 aagattttgc caatgtgaat gcatttcgtc tcctgaacaa gtatcgaaac cagtattgca
 901 cattcaatga tgatattcaa ggaacagcat ctgttgcagt tgcaggtctc cttgcagctc
 961 ttcgaataac caagaacaaa ctgtctgatc aaacaatact attccaagga gctggagagg
1021 ctgccctagg gattgcacac ctgattgtga tggccttgga aaaagaaggt ttaccaaaag
1081 agaaagccat caaaaagata tggctggttg attcaaaagg attaatagtt aagggacgtg
1141 cttccttaac acaagagaaa gagaagtttg cccatgaaca tgaagaaatg aagaacctag
1201 aagccattgt tcaagaaata aaaccaactg ccctcatagg agttgctgca attggtggtg
1261 cattctcaga acaaattctc aaagatatgg ctgccttcaa tgaacggcct attatttttg
1321 ctttgagtaa tccaactagc aaagcagaat gttctgcaga gcagtgctac aaaataacca
1381 agggacgtgc aatttttgcc agtggcagtc cttttgatcc agtcactctt ccaaatggac
1441 agaccctata tcctggccaa ggcaacaatt cctacgtgtt ccctggagtt gctcttggtg
1501 ttgtggcgtg tggattgagg cagatcacag ataatatttt cctcactact gctgaggtta
1561 tagctcagca agtgtcagat aaacacttgg aagagggtcg gctttatcct cctttgaata
1621 ccattagaga tgtttctctg aaaattgcag aaaagattgt gaaagatgca taccaagaaa
1681 agacagccac agtttatcct gaaccgcaaa acaaagaagc atttgtccgc tcccagatgt
1741 atagtactga ttatgaccag attctacctg attgttattc ttggcctgaa gaggtgcaga
1801 aaatacagac caaagttgac cagtaggata atagcaaaca tttctaactc tattaatgag
1861 gtctttaaac ctttcataat ttttaaaggt tggaatcttt tataatgatt cataagacac
1921 ttagattaag attttacttt aacagtctaa aaattgatag aagaatatcg atataaattg
1981 ggataaacat cacatgagac aattttgctt cactttgcct tctggttatt tatggtttct
2041 gtctgaatta ttctgcctac gttctcttta aaagctgttg tacgtactac ggagaaactc
2101 atcattttta tacaggacac taatgggaag accaaaatta ctaataaatt gaaataacca
2161 acattaaaac tcataattat tttgttgacc attttgttaa aatctacttt tc
```

(SEQ ID NO: 7)

Fig. 29

CCTGAAAACACTTTATAACGGGGTAGGGGCAATTATACATAGCAAACGCCGTCAACATTT

AAACTCTAATTTAAACATTTAATTCTTCAGAATTAATACACACAGATGCTATCATGGGGG

GGGGGAGGCGTGCAGCCCCCATCGGGACCGGGTTTTGACAACTTACTTACAACTTTATTA

CATCCTTTTATTTACTGGTCCAGGCGCCGGAGCATGGAAAGATATACAGCGTGGAGTAAA

CACATTCATCCTGGGTGAGGAGTTCTGGCAGGAGACACTGCTTTTCAACATTAAAAATGT

ATAAGGTGTTTAGCAAAAGTTACAGAAAACGGACCAAATGAGCAAGTTTATTTTGTTAGA

AAATTCCACTTTCGTGGGGTTCGCTGATGTGCTCGGGTTGCAAGGGAATGCTTCCGG

(SEQ ID NO: 8)

Fig. 30

```
   1 gttgcagagc agtactgccg ggaacaagaa actgcagcgg gcgctagagg ggcggacctg
  61 aggtcgcgga ttccgaagcc ccggaggcag attccgagtg cagtgggtag gaggctgtcc
 121 tccgggcctc gccgaccatc ctgcggacgg actgggcgtg gccggaggaa ctgtcccgaa
 181 gctgtggggc ctttcatttg gccttgggaa gagcagcagg agaaggcggg gctcctcccc
 241 acgtttcggc cgaagtggct gcagagctga aggggtgggg cctcggggta gcccggtgag
 301 tggatcctgt cctctctcct cagccctgga ccatagccag cacacactga ggcaggaatg
 361 gccccgagac ctccgacggc caagccccag gagtcggtga cattcaaaga tgtggctgtg
 421 aacttcaccc aggaagaatg gcaccacgtg ggccctgccc agaggagctt atacagggat
 481 gtcatgctgg agaactacaa ccacctggtg tcgctcgggt atcaagtctc caagccagag
 541 gtgatcttca aattggagca aggagaagag ccatggatat cagagaaaga aatccaaaga
 601 cctttctgtc cagactggaa gaccaggcct gagtcctcac ggagtcctca gcagggcgta
 661 tctgaagtat tcctcagaac aaatgtttta tcacacacca caataggtga tatctggaat
 721 gtcgctatcc aggggcatca ggaaagtggg agaagacatc tggggccaga ggcatcttcc
 781 cagaagaaaa taaccactct agagaaaaaa attgagcaaa acaaagttgg tgaagactct
 841 agtttgagca cagacttggt tccacaactg gacatttctt caagtataag gcccagtgac
 901 tgtaaaacat ttggaaataa tttggaacac aattcagaac tagttactca gagtaatatc
 961 cttgctaaaa agaagcctta taagtgtgat aaatgtagga aatcatttat tcatagatca
1021 tcacttaata aacacgagaa gattcataaa ggcgatcctt actccaatgg tacagaccaa
1081 ggagctcagt ctggaaggaa acaccatgag tgtgcggact gtgggaaaac cttcctctgg
1141 agaacacagc tcacggagca ccagagaatt cacactgggg aaaaaccctt tgagtgtaat
1201 gtgtgtggaa aggccttcag gcacagctcg tcccttggtc agcatgaaaa cgcacataca
1261 ggagagaagc cctatcagtg tagcctctgt gggaaagcct tccagcgcag ttcatctctt
1321 gttcaacacc agagaatcca cacgggagag aagccctatc gctgcaatct ctgtgggagg
1381 tcattcaggc acagcacgtc cctcacgcaa catgaggtga cccacagtgg ggagaaaccc
1441 ttccagtgta aggaatgtgg gaaggccttt agcaggtgtt cttcccttgt ccagcatgag
1501 aggacccata caggagagaa gcctttcgag tgcagcattt gtgggagggc atttggtcag
1561 agcccatccc tttataaaca tatgaggatt cataaaagaa gcaaacctta ccaaagtaac
1621 aacttcagcc tggcttttgt gcctaacact cctcttcctc aaggtgaagg cctgcttact
1681 gaagtaaagt cgtaccattg taatgactgt gggaaagact tcggtcacat tacagacttc
1741 tctgagcacc agaggctcca cgctggggag aattcctacg gctctgaaca gacccttctt
1801 ggtcagcagt ccctgtctca tccccgagag aaaccctatc agtgcaacgt atgtgggaaa
1861 gcttttaaaa ggagtacaag ttttatagag catcatcgaa ttcacactgg agagaaaccc
1921 tatgaatgta atgagtgtgg ggaagccttc agtcgactct cgtcactcac gcaacacgag
1981 aggacccaca ctggcgagaa accctatgag tgcattgact gcgggaaagc cttcagtcaa
2041 agctcatccc tgattcagca cgaaaggacg cataccggag agaaacccta tgagtgtaat
2101 gagtgtgggc gggcctttag aaagaagacc aatttgcacg accatcagag aactcacact
2161 ggagagaaac cctatgcttg caaggagtgt gggagaaact tcagccggag ctccgccctt
2221 actaaacacc accgagttca cgcccggaat aaactgcagg aaagctaaac aatgggatgg
2281 ggaggaggca cggccgaaca tctgcttcca acccagtgtc agaggattct gaaagtctga
2341 gaatgtaatt atgtgtttgg acactgtgta tagagaaaac tgccactaga agaaaaaaat
2401 tttaaattaa agccattctt tcatacctta ttacaggctt cttgtagaac tacgtacggc
2461 atatgtagtc gtttggaaat gatgtgacct tactaaagct tttgaatata tgtgtgcaga
2521 gtcaccaagt tttaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa
2581 aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaa
```

(SEQ ID NO: 9)

Fig. 31

```
   1 maprpptakp qesvtfkdva vnftqeewhh vgpaqrslyr dvmlenynhl vslgyqvskp
  61 evifkleqge epwisekeiq rpfcpdwktr pessrspqqg vsevflrtnv lshttigdiw
 121 nvaiqghqes grrhlgpeas sqkkittlek kieqnkvged sslstdlvpq ldisssirps
 181 dcktfgnnle hnselvtqsn ilakkkpykc dkcrksfihr sslnkhekih kgdpysngtd
 241 qgaqsgrkhh ecadcgktfl wrtqltehqr ihtgekpfec nvcgkafrhs sslgqhenah
 301 tgekpyqcsl cgkafqrsss lvqhqrihtg ekpyrcnlcg rsfrhstslt qhevthsgek
 361 pfqckecgka fsrcsslvqh erthtgekpf ecsicgrafg qspslykhmr ihkrskpyqs
 421 nnfslafvpn tplpqgegll tevksyhcnd cgkdfghitd fsehqrlhag ensygseqtl
 481 lgqqslshpr ekpyqcnvcg kafkrstsfi ehhrihtgek pyecnecgea fsrlssltqh
 541 erthtgekpy ecidcgkafs qsssliqher thtgekpyec necgrafrkk tnlhdhqrth
 601 tgekpyacke cgrnfsrssa ltkhhrvhar nklqes
```

(SEQ ID NO: 10)

Fig. 32

```
   1 ctggcagcgg actttgaata gggaagtttt gcaggggtta cgcttgcagt cagtccgctg
  61 tttgcaaata ttgcgtgggc tcggcgcgct gcgggctgcg ggagggtccg gacccggcgt
 121 ccgattgcag cgccatccag tttgcatgaa actttcacct gcgctcccgg gaacagtttc
 181 tgctcggact cctgatcgtt cacctccctg ttttcccgac agcgaggact gtcttttcca
 241 acccgacatg gatgtgctcc caatgtgtag catcttccag gaactacaga ttgtgcacga
 301 aacgggctac ttctcggctc tgccgtccct ggaggaatat tggcaacaga cctgcctgga
 361 gttggaacgc tatcttcaga gtgagccctg ctacgtgtca gcctctgaga taaaatttga
 421 cagccaggaa gacctgtgga ccaaattcat tctagctcgg gagaagaagg aggaatcaga
 481 actgaagatt tcttctagtc ccccagagga ctctctgatc agctccagct ttaattataa
 541 cttagagacc aatagcctga actctgatgt cagcagtgag tcttcggaca gttcagagga
 601 actttcaccc acgaccaaat ttacctctga tcccattggt gaagtcttag tcaattcagg
 661 aaatctgagt tcctccgtca tttccacacc tccatcttct ccagaagtga acagggaatc
 721 ttctcaacta tggggctgtg ggccaggaga cctgccctca cctgggaagg ttcgaagtgg
 781 gacctctggg aagtctggtg acaagggtaa tggcgacgcc tccccagatg gcagaagacg
 841 ggtacatcgg tgccacttta atggctgcag gaaagtttac acgaaaagct cccacttgaa
 901 agcacatcag cgcactcaca caggagaaaa gccttacaga tgctcatggg aaggttgtga
 961 gtggcgtttt gcaagaagtg atgagttgac cagacacttc cgaaagcata ccggtgccaa
1021 gccttttaaa tgctcccact gtgacaggtg tttctccagg tctgaccacc tggccctgca
1081 catgaagagg cacctctgaa ggagcagagg gacgaatcct gtaggctaaa agaggcttcc
1141 aggctaagag gcggccatgg aaggagggat gcctgtaaca gccaaagcat gccattttgc
1201 ttcctatcca gttacctcca ggggcctctc tttggaaggt cttttgaggg ctacaaaagt
1261 catgtcagga gtggcatagc acccatggtg catggtgttt gggtgacccc ggactcacca
1321 ctggttccta accttctgag aggctctaag cttttggccg tgagcatgcg cactgagaat
1381 gttagtgggt gggatggttg tgttgaggat ctattactga ctgtatggtg aggcagactt
1441 ttttttctc cccctatgtg gtatcaaata actcgcggct gcagtcttta agaaatagaa
1501 atggcttcca aaagagctct ggtcatcctg gccaaaggag cagtcgacgc ggccgc
```

(SEQ ID NO: 11)

Fig. 33

```
   1 ggatgagaca gaaggataga gaggaggaga gagagagaga gaagagaagc aaccagaaat
  61 aggcagccaa taaaaaggag ccgcacttat ctgaagcctc aaggggcctg agccaggtcc
 121 ctgtttgatg gcagttatga aaaattacct cctcccgatc ctggtgctct ccctggccta
 181 ctactactat tctacaaatg aagagttcag accagaaatg ctccagggaa agaaagtgat
 241 tgtcactggg gccagcaaag ggattggaag agaaatggca tatcatctgt caaaaatggg
 301 agcccatgtg gtattgactg ccaggtcgga ggaaggtctc cagaaggtag tgtctcgctg
 361 ccttgaactc ggagcagcct ctgctcacta cattgctggc actatggaag acatgacatt
 421 tgcggagcaa tttattgtca aggcgggaaa gctcatgggc ggactggaca tgcttattct
 481 aaaccacatc actcagacct cgctgtctct cttccatgac gacatccact ctgtgcgaag
 541 agtcatggag gtcaacttcc tcagctacgt ggtcatgagc acagccgcct tgcccatgct
 601 gaagcagagc aatggcagca ttgccgtcat ctcctccttg gctgggaaaa tgacccagcc
 661 tatgattgct ccctactctg caagcaagtt tgctctggat gggttctttt ccaccattag
 721 aacagaactc tacataacca aggtcaacgt gtccatcact ctctgtgtcc ttggcctcat
 781 agacacagaa acagctatga aggaaatctc tgggataatt gacgccctag cttctcccaa
 841 ggaggagtgc gccctggaga tcatcaaagg cacagctcta cgcaaaagcg aggtgtacta
 901 tgacaaattg cctttgactc caatcctgct tgggaaccca ggaaggaaga tcatggaatt
 961 tttttcatta cgatattata ataaggacat gtttgtaagt aactaggaac tcctgagccc
1021 tggtgagtgg tcttagaaca gtcctgcctc atacttcagt aagccctacc cacaaaagta
1081 tctttccaga gatacacaaa ttttggggta cacctcatca tgagaaattc ttgcaacact
1141 tgcacagtga aaatgtaatt gtaataaatg tcacaaacca ctttgggcct gcagttgtga
1201 acttgattgt aactatggat ataaacacat agtggttgta tcggctttac ctcacactga
1261 atgaaacaat gataactaat gtaacattaa atataataaa ggtaatatca acttcgtaaa
1321 tgcaaaaaaa aaaaaaaaaa aaaaaaaaaa
```

(SEQ ID NO: 12)

Fig. 34

```
   1 mavmknyllp ilvlflayyy ystneefrpe mlqgkkvivt gaskgigrem ayhlskmgah
  61 vvltarseeg lqkvvsrcle lgaasahyia gtmedmtfae qfivkagklm ggldmlilnh
 121 itqtslslfh ddihsvrrvm evnflsyvvm staalpmlkq sngsiaviss lagkmtqpmi
 181 apysaskfal dgffstirte lyitkvnvsi tlcvlglidt etamkeisgi inaqaspkee
 241 caleiikgta lrksevyydk spltpillgn pgrkimeffs lryynkdmfv sn
```

(SEQ ID NO: 13)

Fig. 35

```
   1 gagacggacg gtggccaccc caagacgcgc cccagcccgc catggcccgg atcctccggg
  61 catcctgcct tctgtccctg ctcctggccg ggtttgttcc gccgggccgg ggacaagaga
 121 agtctaagac agactgccat ggcggtatga gtggtaccat ctacgagtat ggagccctca
 181 ccatcgatgg ggaggaatac attcctttta agcagtatgc aggcaaatat atcctctttg
 241 tcaacgtagc cagctactga ggtctgacag accaatacct tgaactgaat gcactacaag
 301 aagaacttgg gccatttggc ttggtcattc tgggcttccc ttccaaccaa tttggcaaac
 361 aggagccagg cgagaactcg gagatactcc ccagtctcaa gtatgttcga ccaggtgggg
 421 gctttgtgcc taatttccag ctctttgaga aaggagatgt gaacggggag aaagagcaga
 481 aattctacac tttcctgaag aactcctgcc ctcccactgc agaactcctg ggctcacctg
 541 gccgcctctt ttgggaaccc atgaagatcc atgacatccg ctggaacttt gagaagttcc
 601 tggtggggcc agatggcata ccggttatgc gctggtacca ccggaccaca gtcagcaacg
 661 tcaagatgga catcctgtct tacatgaggc ggcaggcagc cctgagcgcc agggggaagt
 721 aactgatgcc cccaccctac ccctaccccc tgcccatcat gcaagggccg aggaggggct
 781 cttcaggaag gaagccacat tcccagtcat tctaccccca ccccagattc tctttcttat
 841 tacataaaag acaagcctgg cacaactgtg tgtctgaacc actgtggaca cgtgacaatt
 901 gtcccagtgt gtgcatggct acacagccac gtatctgcct gcttgaaacc cagggatggt
 961 ccatctgtgt ttacggcttg gcacaacacc ctcatatttt tttcagcttt ctgttccaaa
1021 tgagcccaaa ggaaacacaa gttctaggtc caatggttct gctcaaacct gaacatcatt
1081 cttggggcca gcatctccca catgcccaca ctacacacca ccagcctcct tcttccttcc
1141 tgaaggaccc tcctgagccc ccaagcccat cccacagtgc tcctgagacc agccaagaca
1201 actgtgagcg cgatggccgt gtaccccagg tcaggggtgg tgtctctatg aaggaggggc
1261 ccgaagccct tgtgggcggg cctcccctga gcccgtctgt ggtgccagcc cttagtgcat
1321 tcaggcttag gctcccaggc agggacacta cccccgcgcc tctggaggac atgctatcct
1381 ctcactctgt ccactggtat ctcaacaccc ccatctgccc agtaaaggtc tttctgc
```

(SEQ ID NO: 14)

Fig. 36

```
  1 marilrascl lslllagfvp pgrgqekskt dchggmsgti yeygaltidg eeyipfkqya
 61 gkyilfvnva syugltdqyl elnalqeelg pfglvilgfp snqfgkqepg enseilpslk
121 yvrpgggfvp nfqlfekgdv ngekeqkfyt flknscppta ellgspgrlf wepmkihdir
181 wnfekflvgp dgipvmrwyh rttvsnvkmd ilsymrrqaa lsargk
```

(SEQ ID NO: 15)

Fig. 37

```
   1 ctgtaaagcc ccgcctcagc cccgcccccc cgtcccgccc gccgcgggcc aagccggagc
  61 aagctaggag gcagccggct ctgcggaggc aacatgtacc ggctcctgtc aagcgtgaca
 121 gctcgggctg cggccaccgc aggcccagcc tgggacggag ggcggcgcgg ggcgcacagg
 181 cgaccgggcc tgcctgtgct gggccttggt tgggccggcg gcctggggct cgggctgggg
 241 ctggctctcg gcgcgaagct ggtggtcggg ctgcggggcg ccgtccccat tcagtccccc
 301 gcggaccccg aggcgtccgg cactaccgag ttatcgcacg agcaggccct gagcccgggg.
 361 agcccgcaca cgcctgcgcc gccagcagcc aggggcttct ccagagccat cgagagcagc
 421 cgcgatctgc tacaccggat caaggatgag gttggtgccc ccggcatcgt ggttggagtt
 481 tctgtagatg gaaaagaagt ctggtcagaa ggtttaggct atgcagacgt ggagaaccgc
 541 gtaccctgta agccagaaac ggtcatgaga atcgcaagca tcagcaaaag cctcaccatg
 601 gtggctctgg ctaaactgtg ggaagcaggg aagctggatc tggaccttcc tgtgcagcac
 661 tatgttcccg agttcccaga aaaagaatac gagggtgaaa aggtttctgt cacaacaaga
 721 ttactaattt cgcatttaag tggaattcgt cattatgaaa aggacataaa gaaagtgaaa
 781 gaagagaaag cttataaagc cctgaagatg gtgaaaggga ccccgccacc atctgaccaa
 841 gaaaaagaac tgaaagaaaa gggaggcaaa aacaacgaaa agagcgacgc accgaaagcc
 901 aaagtcgagc aggacagcga agccagatgc cgcagcgcga agccaggcaa gaaaaagaat
 961 gacttcgaac aaggcgaatt gtatttgaaa gaaaagtttg aaaattcaat tgaatcacta
1021 agattattta aaaatgaccc tttattcttt aaacctggta gtcagttttt gtattcaacg
1081 tttggctata ctctgctggc agccatagta gaaagagctt caggatataa atatttggat
1141 tatatgcaga aaattttcca tgatttggac atgctgacaa ctgtccagga ggaaaacgag
1201 ccagtgattt acaacagagc aagattttac gtgtacaata aaaagaaacg tcttgtcaac
1261 acaccttacg tggataactc ctataaatgg gctggtggtg gatttctgtc cacagtgggt
1321 gacctcctga aatttggaaa cgcaatgctg tatggctacc aagttgggca gtttaagaac
1381 tcaaatgaaa atctcttgcc tggatatctc aagccagaaa caatggtgat gatgtggacc
1441 ccagtcccta acacagagat gtcctgggat aaagagggga aatatgcaat ggcgtggggt
1501 gtggtagaga agaagcaaac gtacggatcc tgcaggaagc agcggcacta cgcctcacat
1561 actggaggtg ctgtgggtgc cagtagtgtc ctgctggtcc ttcctgaaga actggactca
1621 gaggccgtaa ataacaaggt tcccccacga ggaataatcg tctctatcat atgcaacatg
1681 cagtctgtgg ggctcaatag cactgctttg aagatcgctc tggaatttga taaagacaga
1741 gctgactaat cctaatggca gcacaggtcc acagtgagcc ttccattctt tgaaatgttg
1801 acgttcccaa atacataaac cctttaagga tacatttcgt tcccaaatac ataaaccctt
1861 taaggataca tttgtaatag agtacagtta aatgtggaga attatgtacc tctaattgct
1921 taattttgta actgcctttt tattggacaa ttagttcttt acactcaggg aaataacagt
1981 tgtttctact ttttaaaaaa aatgtttact cttgaaataa aatcttctga t
```

(SEQ ID NO: 16)

Fig. 38

```
  1 myrllssvta raaatagpaw dggrrgahrr pglpvlglgw agglglglgl algaklvvgl
 61 rgavpiqspa dpeasgttel sheqalslgs phtpappaar gfsraiessg dllhrikdev
121 gapgivvgvs vdgkevwseg lgyadvenrv pckpetvmri asisksltmv alaklweagk
181 ldldlpvqhy vpefpekeye gekvsvttrl lishlsgirh yekdikkvke ekaykalkmv
241 kgtppppdqe kelkekggkn neksdtpkak aeqdsearcr sakpgkkknd feqgelylke
301 kfensieslr lfkndplffk pgsqflystf gytllaaive rasgykyldy mqkifhdldm
361 lttvqeenep viynrarfyv ynkkkrlvnt pyvdnsykwa gggflstvgd llkfgnamly
421 gyqvgqfkns nenllpgylk petmvmmwtp vpntemswdk egkyamawgv vekkqtygsc
481 rkqrhyasht ggavgassvl lvlpeeldse avnnkvpprg iivsiicnmq svglnstalk
541 ialefdkdra d
```

(SEQ ID NO: 17)

Fig. 39

```
   1 aggctgnnag ccacacttgg gaaaggaagc atggcgtgcg agctgcgagc tgtgttgctg
  61 tggggccgcg ggctgcagac tgtactgcgg gcccccgcgc tggctggagt tcggcgagga
 121 aagccagttc tgcaccttca gaagactaca gtccagttta ggggccccac acaaagtctg
 181 gcttcaggga tctctgcagg acagttatac agcacacagg cagccgagga caaggaggag
 241 gagagcctgc actccatcat cagcaacact gaggcagtgc ggggttctgt ctccaaacat
 301 gagttccagg cagagacaaa gaaacttttg gacatcgtag cccgttctct gtactcagaa
 361 aaagaggtgt tcatacgaga gctcatctcc aatgccagtg atgccttgga gaaactgcgg
 421 cacaagctgg tgtgtgaagg ccaggtgctg ccagaaatgg agattcacct tcagacggat
 481 gccaagaagg gcactattac cattcaggac actggcattg ggatgacaca ggaggagctg
 541 gtgtccaacc ttggcacaat tgccagatcg gggtcaaagg ccttcctgga agcactgcag
 601 aaccaggcag agaccagcag caagatcatt ggtcagtttg gagtgggttt ctattcagcc
 661 ttcatggtag ctgacaaggt tgaagtctat tctcgatcag cagctccaga gagcccaggt
 721 taccagtggc tttcagatgg ttctggagtg tttgaaattg ccgaagcttc aggagttaga
 781 cctgggacca aaataatcat ccacctcaag tcagactgta aagattttgc cagcgagtcc
 841 cgggtacaag atgtggtaac aaagtacagt aactttgtca gcttcccctt gtaccttaat
 901 ggaaagcgga ttaacacttt gcaggccatc tggatgatgg acccaaagga catcagtgaa
 961 tttcagcatg aggaattcta ccgttatatt gctcaggctt atgataagcc ccgcttcact
1021 ttgcactaca agacggacgc accactcaac atccgcagca tctttctatgt gccagagatg
1081 aaaccatcca tgtttgatgt gagcagggag ctgggctcca gcgtggcact gtatagccgc
1141 aaggtcctca tccagaccaa ggctgcagac atcctgccca agtggctgcg cttcattcga
1201 ggtgtggtgg atagtgagga cattcccctg aacctcagca gagagctcct gcaggagagt
1261 gcgctcatcc ggaaactccg ggatgttcta caacagagat tgatcaagtt cttcattgac
1321 cagagtaaaa aagatgctga aaaatacgca aagtttttg aagattatgg cttgttcatg
1381 agggagggca ttgtgaccac tgcagagcaa gacatcaagg aggatattgc aaaactgcta
1441 cggtatgagt cctcagccct gcctgctggg cagctgacca gcttaccaga ctatgccagc
1501 cgaatgcagg ctggcacccg caacatctat tacctgtgtg cccctaaccg tcacctggct
1561 gaacattcac cctattacga agccatgaag cagaaacata ctgaggtgct cttctgctat
1621 gagcagttcg atgagcttac tctgctgcac ctgagggagt ttgacaagaa gaagctcatc
1681 tctgtggaaa cagacatcgt cgttgatcac tacaaggagg aaaagtttga ggacacatct
1741 ccagctgatg agcgcctctc ggagaaggaa acagaagatc taatggcgtg gatgagaaat
1801 gcactagggt cccgtgtcac caatgtgaag gtgactttcc gcctagacac ccaccctgcc
1861 atggtgaccg tgctggagat gggggctgct cggcatttct tgcgtatgca gcagctggcc
1921 aagacccagg aggaacgtgc ccaactgcta cagcccacac tggagatcaa ccccaggcac
1981 acactgataa agaagctctg ccagctgagg gagagcgagc cggagctggc ccagctgctc
2041 gtggatcaga tctatgagaa tgccatgata gcagcaggac tcgttgatga cccccgggcc
2101 atggtcggcc gcctgaacga ccttttggtc aaggtcctgg agaaacactg acagccaaga
2161 cactggattt agtgtcaacc caggtcttct cgggtgataa tggacctgcc tggggaggca
2221 ggacttaata cacaaacagt gccaccaact gcttgagctc agctttattt acttcaatta
2281 aacagtattt cttagtc
```

(SEQ ID NO: 18)

Fig. 40

```
  1 acelravllw grglqtvlra palagvrrgk pvlhlqkttv qfrgptqsla sgisagqlys
 61 tqaaedkeee slhsiisnte avrgsvskhe fqaetkklld ivarslysek evfirelisn
121 asdaleklrh klvcegqvlp emeihlqtda kkgtitiqdt gigmtqeelv snlgtiarsg
181 skaflealqn qaetsskiig qfgvgfysaf mvadkvevys rsaapespgy qwlsdgsgvf
241 eiaeasgvrp gtkiiihlks dckdfasesr vqdvvtkysn fvsfplylng krintlqaiw
301 mmdpkdisef qheefyryia qaydkprftl hyktdaplni rsifyvpemk psmfdvsrel
361 gssvalysrk vliqtkaadi lpkwlrfirg vvdsedipln lsrellqesa lirklrdvlq
421 qrlikffidq skkdaekyak ffedyglfmr egivttaeqd ikediakllr yessalpagq
481 ltslpdyasr mqagtrniyy lcapnrhlae hspyyeamkq khtevlfcye qfdeltllhl
541 refdkkklis vetdivvdhy keekfedtsp aderlseket edlmawmrna lgsrvtnvkv
601 tfrldthpam vtvlemgaar hflrmqqlak tqeeraqllq ptleinprht likklcqlre
661 sepelaqllv dqiyenamia aglvddpram vgrlndllvk vlekh
```

(SEQ ID NO: 19)

Fig. 41

```
   1 ctccgcgtcc gccccgccac cgtgccagcc atggagcccc gagcccccg ccgccgacac
  61 acccaccagc gcggctacct gctgacgcgg gacccgcatc tcaacaagga cttggctttt
 121 actctggaag agagacagca gttgaacatt catggattgt tgccgccctg catcatcagc
 181 caggagctcc aggtccttag aataattaag aatttcgaac gactgaactc tgacttcgac
 241 aggtatctcc tgttaatgga cctgcaagac agaaatgaga agctcttcta cagcgtgctc
 301 atgtctgatg ttgaaaagtt catgcctatt gtttacaccc ccaccgtggg cctcgcatgc
 361 cagcagtaca gtttggcatt ccggaagcca agaggcctct ttattagtat ccatgacaaa
 421 gggcacattg cttcagttct taatgcatgg ccagaggatg tcgtcaaggc tattgtggta
 481 actgatggag agcgcatcct tggcttggga gaccttggct gtaatgggat gggcatccct
 541 gtgggtaaac tggccctgta cacggcatgt ggaggggtga acccacaaca gtgtctaccc
 601 atcactttgg atgtgggaac agaaaatgag gagttactta aggatccact gtacatcggg
 661 ctgcggcacc ggcgagtcag aggccctgag tatgacgcct tcctggatga gttcatggag
 721 gcagcgtctt ccaaatatgg catgaattgc cttattcagt ttgaagattt tgccaatcgg
 781 aatgcatttc gtctcctgaa caagtatcga aacaagtatt gcacatttaa cgatgatatt
 841 caaggaacag cgtctgttgc ggttgcgggt ctccttgcag ctcttcgaat aaccaagaac
 901 aagctctctg atcagacagt gctgttccag ggagctggag aggctgcctt ggggattgct
 961 cacttggttg ttatggccat ggagaaagaa ggtttatcaa aggagaatgc tagaaagaag
1021 atatggttgg ttgactcaaa aggactaata gttaagggtc gtgcatctct cacagaagag
1081 aaagaggtgt ttgcccatga acatgaagaa atgaagaatc tggaagccat tgttcaaaag
1141 ataaaaccaa ctgccctcat aggagttgct gcaattggtg gtgctttcac tgaacaaatt
1201 ctcaaggata tggctgcctt caacgagcgg cccatcatct ttgctttgag taatccgacc
1261 agcaaagcgg agtgctctgc agagcagtgc tacaaggtga ccaagggacg tgcaatcttt
1321 gccagcggca gtccttttga tccagtcact ctcccagatg gacggactct gtttcctggc
1381 caaggcaaca attcctacgt gttccctgga gttgctcttg gggtggtggc ctgcggactg
1441 agacacatcg atgataaggt cttcctcacc actgctgagg tcatatctca gcaagtgtca
1501 gataaacacc tgcaagaagg ccggctctat cctcctttga ataccattcg aggcgtttcg
1561 ttgaaaattg cagtaaagat tgtgcaagat gcatacaaag aaaagatggc cactgtttat
1621 cctgaacccc aaaacaaaga agaatttgtc tcctcccaga tgtacagcac taattatgac
1681 cagatcctac ctgattgtta tccgtggcct gcagaagtcc agaaaataca gaccaaagtc
1741 aaccagtaac gcaacagcta ggatttttaa ctttattagt aaaatcttga agttttcatg
1801 atctttaagg gtcagaatct tttatgatga ttcatagtgt gcttagaata aggtgatttt
1861 agtttaataa caaactcatg ggagtctatt aggataaatt aggataaatt tcacaccaga
1921 cggttttgtt tcacttactg tggatattta tgttttctct tgtgattatt ctctttatga
1981 attctgttta aaagctactg tacctgctgc tgagaaagtc ctcactgata tgtaggaagc
2041 taatggaaga cccacactag taataaatta atatagcata acttgattac atttaatgcc
2101 tacagttctt tcttgactat tttgctaaaa tctcttaaac agaaaagata aacacaaact
2161 tgggtatagc tgaactttta ctaaacagaa gcactacttt gttgcctaga gaaaatcttc
2221 tcaggacttt tattccaggc ctccgttagc tttgttctct ttgtacacct gactcaacac
2281 ctctgagaaa gctcactgct gtttacagta ccctgcgtag ccttagctca tcagcgtctt
2341 ctgtcgttgt tatgttatat cccatagagt agagctctcg ttcccaaaca ctccatagaa
2401 acacccttttc tcatctctga gcaacccctg gccctgctga gatactcggg tgtttttgtt
2461 agtgtagcct gggcagtgag aagggctgca ggggggtcct tgagacgggg ccctgggaac
2521 ccacctctga gacaagggag tcagatgcca gacagtggtt cccagacaag ctcaggctcc
2581 atgaagatca cctgctctaa tgtccctgtg cttagttcgg aggactgaga gctcatggca
2641 tgagtaaata catctctaat gcctaccttt ctatcagata ttaaaatatg ttaattacca
2701 aaaccattct ctgagaaaaa aaaaccaagc ctttcccagg tggtattaat ttactggaca
2761 cgttgataat ggcatgacta gaaacagcct taactcctaa gctcaggttc aagaacattc
2821 tgtgtatcta gagactcctg actttgaagt tgctttaaag cctgtgtggg tttgcggcgg
2881 gcagctctgt acagtgagct ccttgaaggt gagggtgcag aagctttcag gtgtgagcta
2941 aaagggtaca gacttcctaa tgacaacttg tgactaacgg tttcttcagt gtagttattt
3001 gagaaagatt cagaatttct atcttttctt gtatgtttcc atgttgtcag gtagttgtaa
3061 atgaatgtat ttacctatgc aaaagattta ttaaagccta gagaat
```

(SEQ ID NO: 20)

Fig. 42

```
   1 ttcccgcgct tctgctccgc cctccgcagc cctccacagt caccccggag accagccgtg
  61 ttaagctctc tgctctgaag ctgactgact tccatggcag ccgcgaagaa agcagttctg
 121 gggccattgg tgggagcagt ggaccagggt accagctcga cacgtttttt ggttttcaat
 181 tcaaaaacag ctgaacttct tagtcatcat caagtagaaa taaaacagga attcccaaga
 241 gaaggatggg tagaacaaga cccgaaggaa attctgcagt ctgtttatga gtgtatagag
 301 aaaacgtgtg agaaacttgg acagctcaat attgatattt ccaacatcaa agccattggt
 361 gtcagcaacc agagggaaac cacagtagtc tgggacaagg tcaccggaga gcctctctat
 421 aatgccgtgg tgtggcttga cctaagaacc cagtctactg ttgagaacct tagtaaaaga
 481 attccaggaa ataataactt tgtcaagtcc aagacaggcc ttccacttag cacgtatttc
 541 agtgcagtga aacttcgttg gctccttgac aacgtgaaaa aggtccaaga ggctgttgaa
 601 gaaaatagag ctctttttgg gaccattgat tcatggctta tttggagttt aacaggagga
 661 atccatgggg gtgtccactg tacagatgta acaaatgcaa gcaggacgat gcttttaac
 721 attcattctt tggaatggga taaagagctc tgcgaatttt ttggaattcc aatggaaatt
 781 cttcccaacg ttcggagttc ttctgagatc tatggcctaa tgaaagctgg ggccttggaa
 841 ggtgtaccaa tatctgggtg tttgggggac cagtctgctg ctttggtggg acaaatgtgc
 901 ttccaggatg gacaggccaa aaacacgtat ggaacagggt gcttcttatt gtgcaacacg
 961 ggccataagt gtgtattttc tgaacatggc ctcctgacaa ccgtagcata taaacttggc
1021 agagacaaac ctgtgtatta tgcgttggaa ggttccgtgg ctatagctgg tgctgtaatc
1081 cgctggctaa gagacaacct tggaattatt aagtcctctg aggaaattga aaaacttgct
1141 aaggaagtag gtacttctta tggctgctac ttcgttccag cattttcagg gttatatgcg
1201 ccttattggg agcccagtgc aagagggatc atctgtggac tcactcagtt caccaataaa
1261 tgtcatatcg cttttgctgc actagaagct gtttgtttcc aaacccgaga gattttggat
1321 gccatgaatc gcgactgtgg aattccactc agtcatttac aggtagatgg aggaatgacc
1381 agcaataaaa ttcttatgca gctacaagca gacattctgt atattccagt agtgaaaccc
1441 tccatgcctg aaacaactgc actaggcgct gccatggcag ctggggctgc agaggggggtt
1501 ggtgtgtgga gtcttgaacc tgaggatttg tcagctgtca caatggagcg gtttgaacct
1561 cagatcaatg ctgaagaaag cgaaatccgt tactccacat ggaagaaagc tgtgatgaag
1621 tcaattggtt gggttacaac tcagtctcca gaaagtggta tcccataaat aataccacct
1681 cacggatttc caagatgcaa gctttttaat gtgatatgaa aatctgacta ttctgtctca
1741 tagtataatg atgctattca tagactctga ttttttttcat aagccactgg ctgcatgatc
1801 ctctaagcag acctatgact tgaaataaag aaagtgcagc agaaagaatc ctccagaaac
1861 atttaatttt tttttaacat tgacagttaa gatcgggtca gtcacctttg aggctgacct
1921 ctgcctccac tgtcatgatg tcctacacta ttcccgttaa ggtctagggt gattttggta
1981 tcctgtctat tgaaatgtgc cattcagtat attcagatgc tagtggatta cacatgtttg
2041 aggaagaggt tgttactaac ctgttcaaaa tgagtggctt cttgcttgtt tgcttttaac
2101 agctcagatg tcttcttttc tatatattag aaggccacaa cattactgga tatttcaaat
2161 ggaaacatct aaagaattgt tggataattg aatttgctaa ttcttgtggc ttaagacatt
2221 tttctgtaca gttgtttgcc caaaattcca accttgtcag gtgttttaca ctgtcccact
2281 aactaccata gctttctgtc tggctcttac aggatagaac actttctttt tctgcttttt
2341 tttcatttct ccttttttata ttttttattct gtatgtataa catacatgcc tatatatttt
2401 atatgctgag agtaacccat ttataaatta agagcacatt atattcaata agttataaga
2461 gggctggtct taagtggact actatgtata cag
```

(SEQ ID NO: 21)

Fig. 43

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  1 maaakkavlg plvgavdqgt sstrflvfns ktaellshhq veikqefpre gwveqdpkei
 61 lqsvyeciek tceklgqlni disnikaigv snqrettvvw dkvtgeplyn avvwldlrtq
121 stvenlskri pgnnnfvksk tglplstyfs avklrwlldn vkkvqeavee nralfgtids
181 wliwsltggi hggvhctdvt nasrtmlfni hslewdkelc effgipmeil pnvrssseiy
241 glmkagaleg vpisgclgdq saalvgqmcf qdgqakntyg tgcfllcntg hkcvfsehgl
301 lttvayklgr dkpvyyaleg svaiagavir wlrdnlgiik sseeieklak evgtsygcyf
361 vpafsglyap ywepsargii cgltqftnkc hiafaaleav cfqtreilda mnrdcgipls
421 hlqvdggmts nkilmqlqad ilyipvvkps mpettalgaa maagaaegvg vwslepedls
481 avtmerfepq inaeeseiry stwkkavmks igwvttqspe sgip
```

(SEQ ID NO: 22)

Fig. 44

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   1 tgtcagactc tcgatttctc ctcctactcc tcctccgagg aattctgcgc cctgtaactg
  61 ttctgccctc ccctttaaag gttgacttgc cctacggcgc tccaccgcgc tccagtcctc
 121 ttgcgcctcc tgctcaaccc gctcctgact gccccacgcc gcgtagttcc agcagcaaag
 181 cagaagggtg caccgggaga tggagagcaa agccctgctc ctggtggtcc tgggagtttg
 241 gctccagagt ttgaccgcct tccgaggagg ggtggccgca gcagacgcag gaagagattt
 301 ctcagacatc gaaagcaaat ttgccctaag gacccctgaa gacacagctg aggacacttg
 361 tcatctcatt cctggattag cagactctgt gtctaactgc cacttcaacc acagcagcaa
 421 gaccttcgtg gtgatccatg gatggacggt aacgggaatg tatgagagtt gggtgcccaa
 481 acttgtggcc gccctgtaca agagagaacc tgactccaat gtcattgtag tagactggtt
 541 gtatcgggcc cagcaacatt atccagtgtc agctggctac accaagctgg tgggaaatga
 601 tgtggccaga ttcatcaact ggatggagga ggagtttaag tacccctag acaacgtcca
 661 cctcttaggg tacagccttg gagcccatgc tgctggcgta gcaggaagtc tgaccaataa
 721 gaaggtcaat agaattactg gtttggatcc agctgggcct aactttgagt atgcagaagc
 781 ccccagtcgc ctttctcctg atgacgctga ttttgtagat gtcttacaca catttaccag
 841 ggggtcacct ggtcgaagta ttgggatcca gaaaccagtg gggcatgttg acatttatcc
 901 caatggaggc actttccagc caggatgcaa cattggagaa gccatccgtg tgattgcaga
 961 gagaggactc ggagacgtgg accagctggt gaagtgctcg catgagcgct ccattcatct
1021 cttcattgac tccctgctga atgaagaaaa ccccagcaaa gcatacaggt gcaactccaa
1081 ggaagccttt gagaaagggc tctgcctgag ttgtagaaag aatcgctgta acaatctggg
1141 ctatgagatc aacaaggtca gagccaagag aagcagcaag atgtacctga agactcgctc
1201 tcagatgccc tacaaagtgt tccattacca agtcaagatt cacttttctg ggactgagaa
1261 tggcaagcaa cacaaccagg ccttcgaaat ttctctgtac ggcacagtgg ccgagagcga
1321 gaacattccc ttcaccctgc ccgaggtttc cacaaataaa acctactcct tcttgattta
1381 cacggaggtg gacatcggag aactgctcat gatgaagctt aagtggatga gcgactccta
1441 cttcagctgg cccgactggt ggagcagccc cagcttcgtc atcgagagga tccgagtgaa
1501 agccggagag actcagaaaa aggtcatctt ctgtgctagg gagaaagttt ctcatctgca
1561 gaagggaaag gactcagcag tgtttgtgaa atgccatgac aagtctctga agaagtctgg
1621 ctgacactgg acaaacaaac aagagaagaa agcatccgag ttctttgaag acagaagaaa
1681 acaaagtaaa tttaatttaa aaaaataata cccttgtttg ggtgtttgaa agtgggtttt
1741 cctgagtatt aatcccagct ctatcttgtt agttaaacag aagacagtct caaatattaa
1801 acggtggcta acccagggtg aggaatctaa tggcccatag caggtcttcc agcatcagaa
1861 gacatcaggc aggagaaaca tgctgtcttg tatcccttaa gaaggaatca tttgttccca
```

Fig. 45A

```
1921 acaatataag actccatcat gtgacccatt tggtcatggt ctaaaattag taagaactct
1981 gaggttttat attgagacct tttcaaagtt ttctcaaagt ctaatataga caatattttt
2041 tgtggcatga gtcaggtcca tttctttagc ggttgaaaca cctggccttt gcaactagtt
2101 ttttttacc attgggatat attcccccca ccaaaaaaaa aaaaaaaaaa aagtaaccag
2161 gaacgtgtga cttggcaaaa gcagttgaag acatggctca tgaagtcctg acccttggtc
2221 ccaccacaac aaagtacaag tcaacagaga tacaaaacct agactgagta attcttaata
2281 gacttgaatt tttatggctt aatccttcta tcttttaaat atttgtcaga tattttaaca
2341 ttgttctctg gatagatgtt gaaaatgagc ttataagctg ggcaatggtg gcgctcacct
2401 ttaatcccag cacttggcag gcagaggcag gcggatttct gagttcaagg ccagcctggt
2461 ttacagagtg agttccagga catccagagc tacacagaga aaccctgtct cgggaaaaaa
2521 aaaaaaaaag aagaagaagg agaagaagag ggagggaggg agggagggag ggagggaggg
2581 aggaaggaag gaaggaagga aggaaggaag gaaggaagga aggaaggaag gaagaaagaa
2641 agaaagaaag aaagaaagaa agaaagaaag aaagaaagaa agaaagaaag aaagaaagaa
2701 aatgagcttg taattgaggt gacacataaa ttttgctgaa agacaaaaat gcctaggttg
2761 attttacttc tctttttgc tttcttgaaa aaagtcacaa ttgtcccatg ctgtaaccaa
2821 gtctggccta gaactaaact atgtatttca ggctggcctt gaactctcaa ccatcctgcc
2881 ttagcttcct gtgtcctggg agcttgagaa ccgtaatttt attatcagat ttttcttact
2941 tgttttcatc aatttgaaat gcccaatatc caatactttg tatttcattt gagactcatc
3001 tccgccatgc ctctgtcaca cttctaacac atcacattaa tttctagttt agatgtgatc
3061 aagttcaaat tctgcactgt gcaaagtaca agttttagag caggaccatt ttttttatca
3121 cataaaagtt gaaattacta gaaaatgtgc atatggatgc ttgtaaactg ctgtgcaaag
3181 agaagagccc tcaactgtaa tagctataga aagtaccagg attgttgccg ctgttttgtt
3241 ttaccttaac aacaacaaca acaaaaatca ataatgaaga attatttatg aacgagatct
3301 cacattttca gattgctttt attattcatt aatgtaaaat gataaagaag atctatctca
3361 gaggctatag ctgggagcag aaactgtgaa atttgtgggt atctgaacac caacccacat
3421 gcaaaacccc acaagtgtag tcgtcattca atgtgattca gaaaggaaag agtcaaggga
3481 tatactggaa tatgttagag aagtagttcc agatatgctg gaatgttagc ccttgctagg
3541 agaaagctgg ttgtgcctat gtaatatagg acaaaggtga ccgatttcat caagtttgga
3601 gtcaattcta acaataaaaa tatgtataat ttgttaccgg catccccatt attgctaatt
3661 cattacagta tatacacatc catgcataca tatgtcaatg atgctttagc tttcaattta
3721 tttattagct gtaaataatg tgtgggtatg taagaatgct tgtaaacact ggaaagtctg
3781 ttgtggttat ctgcagtata gatttgtggt gctaactttg tgtccgtctc catccatgat
3841 tgtctgtctc actgagccaa cttaactctg atgaaacagt acaatgaaat aggcttttga
3901 aagaagaaaa ctcacctgtg tgaagaaatg gtatctgctt tcaataaaac tgagaacatt
3961 ttatcatga
```

(SEQ ID NO: 23)

Fig. 45B

```
  1 meskalllvv lgvwlqslta frggvaaada grdfsdiesk falrtpedta edtchlipgl
 61 adsvsnchfn hssktfvvih gwtvtgmyes wvpklvaaly krepdsnviv vdwlyraqqh
121 ypvsagytkl vgndvarfin wmeeefnypl dnvhllgysl gahaagvags ltnkkvnrit
181 gldpagpnfe yaeapsrlsp ddadfvdvlh tftrgspgrs igiqkpvghv diypnggtfq
241 pgcnigeair viaerglgdv dqlvkcsher sihlfidsll neenpskayr cnskeafekg
301 lclscrknrc nnlgyeinkv rakrsskmyl ktrsqmpykv fhyqvkihfs gtengkqhnq
361 afeislygtv aesenipftl pevstnktys fliytevdig ellmmklkwm sdsyfswpdw
421 wsspsfvier irvkagetqk kvifcarekv shlqkgkdsa vfvkchdksl kksg
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(SEQ ID NO: 24)

Fig. 46

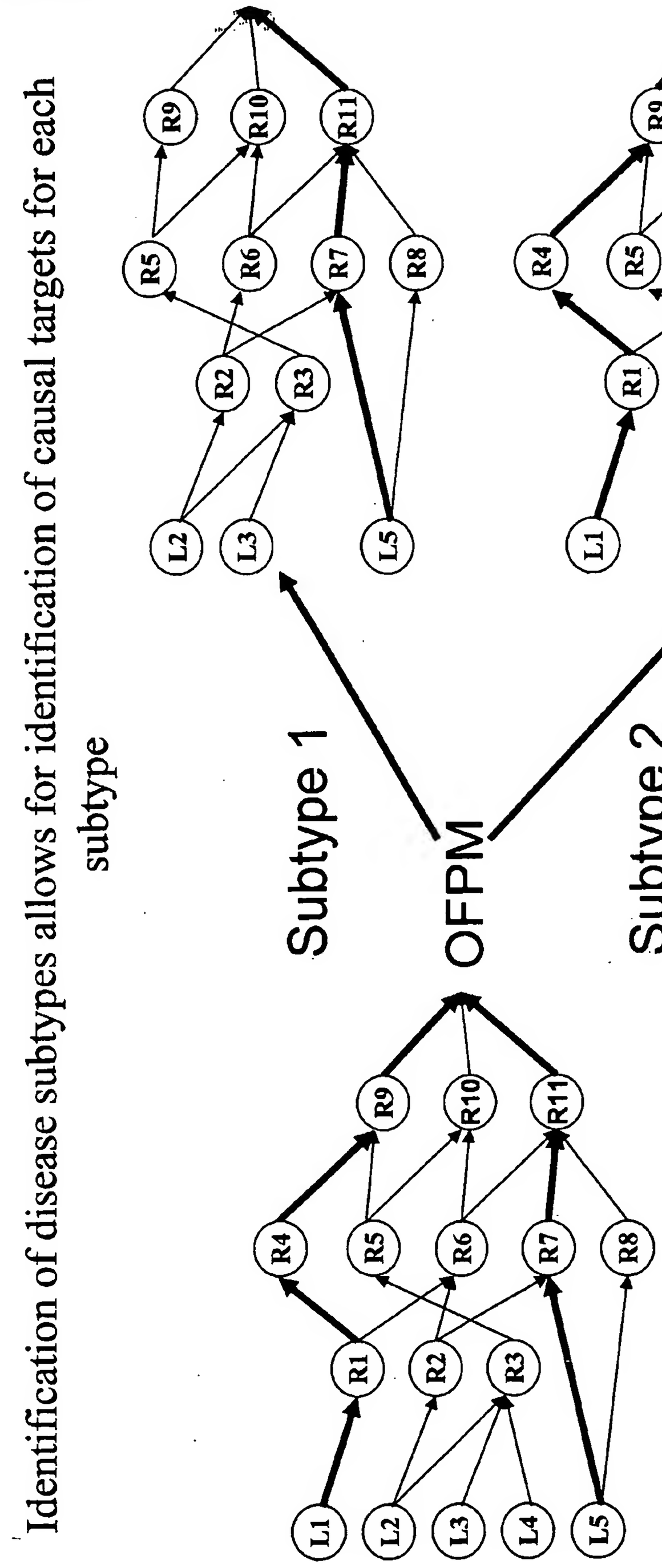
Identification of disease subtypes allows for identification of causal targets for each subtype
L1
L2
L3
L4
L5
R1
R2
R3
R4
R5
R6
R7
R8
R9
R10
R11
OFPM
Subtype 1
Subtype 2

Fig. 47

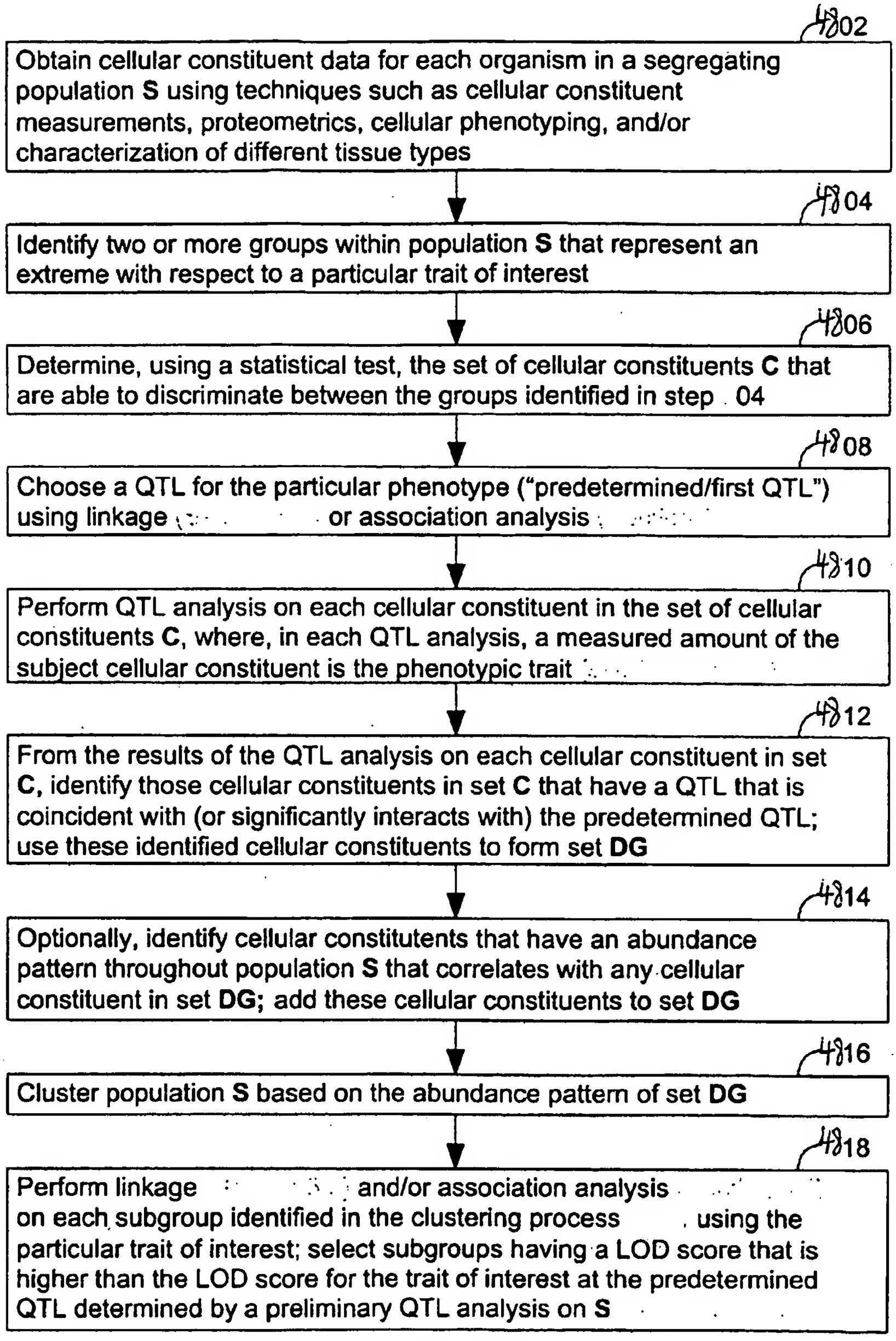
402
Obtain cellular constituent data for each organism in a segregating population S using techniques such as cellular constituent measurements, proteometrics, cellular phenotyping, and/or characterization of different tissue types
404
Identify two or more groups within population S that represent an extreme with respect to a particular trait of interest
406
Determine, using a statistical test, the set of cellular constituents C that are able to discriminate between the groups identified in step 04
408
Choose a QTL for the particular phenotype ("predetermined/first QTL") using linkage or association analysis
410
Perform QTL analysis on each cellular constituent in the set of cellular constituents C, where, in each QTL analysis, a measured amount of the subject cellular constituent is the phenotypic trait
412
From the results of the QTL analysis on each cellular constituent in set C, identify those cellular constituents in set C that have a QTL that is coincident with (or significantly interacts with) the predetermined QTL; use these identified cellular constituents to form set DG
414
Optionally, identify cellular constitutents that have an abundance pattern throughout population S that correlates with any cellular constituent in set DG; add these cellular constituents to set DG
416
Cluster population S based on the abundance pattern of set DG
418
Perform linkage and/or association analysis on each subgroup identified in the clustering process using the particular trait of interest; select subgroups having a LOD score that is higher than the LOD score for the trait of interest at the predetermined QTL determined by a preliminary QTL analysis on S

FIG. 48

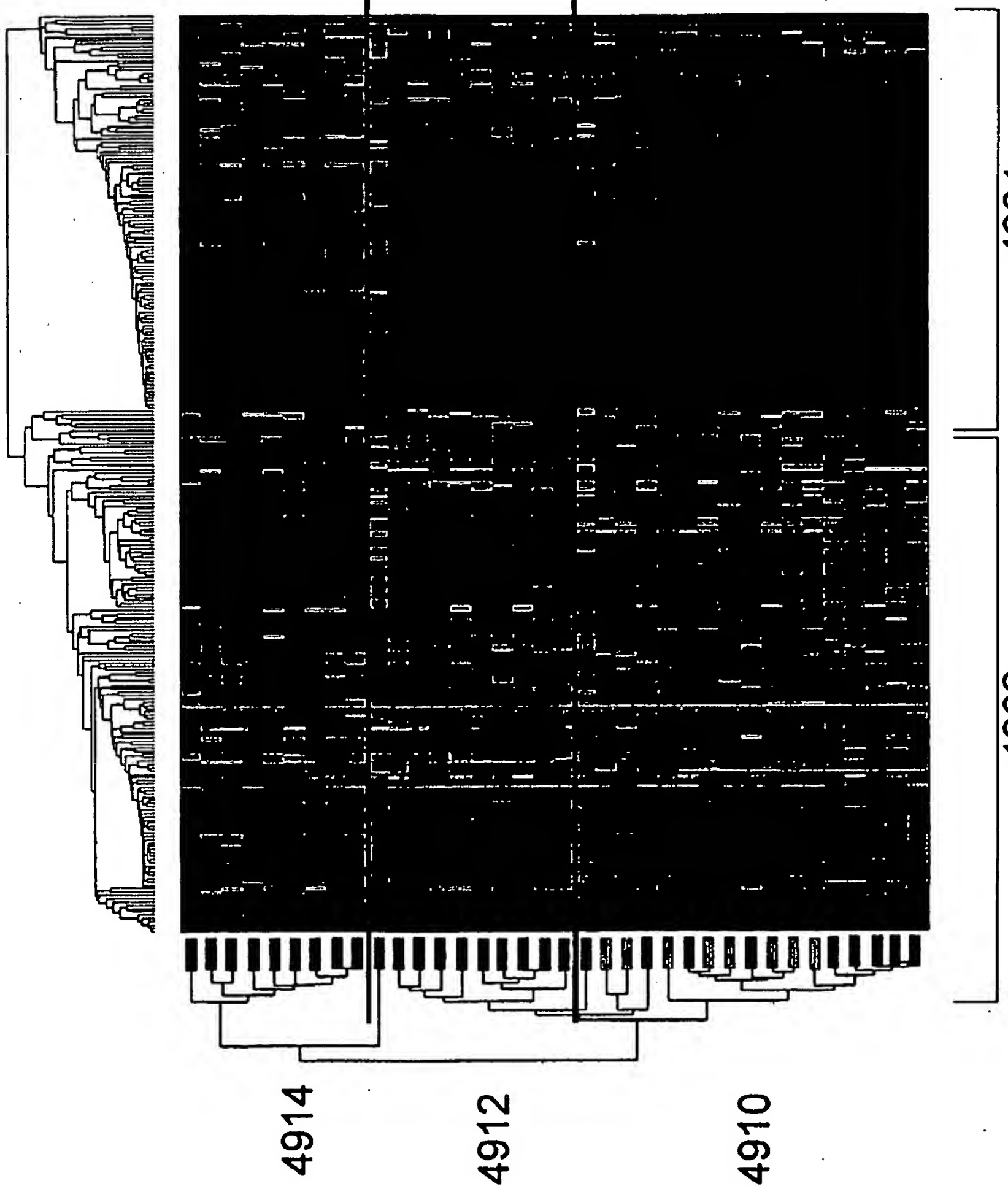
High FPM Group 1
High FPM Group 2
Low FPM Group
4902
4904
4914
4912
4910

Fig. 49

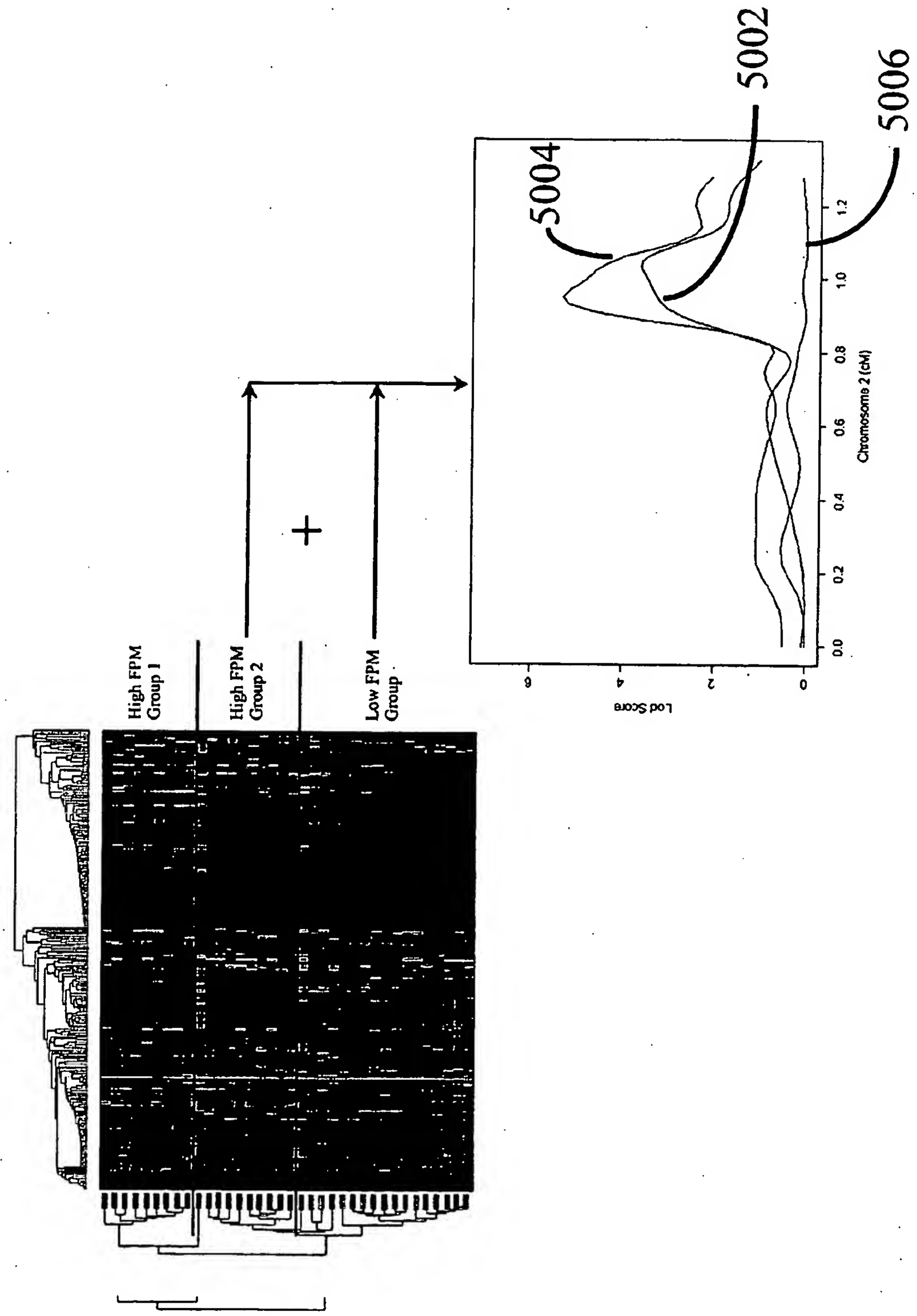
5002
5004
5006
High FPM Group 1
High FPM Group 2
Low FPM Group
Lod Score
Chromosome 2 (cM)

Fig. 50

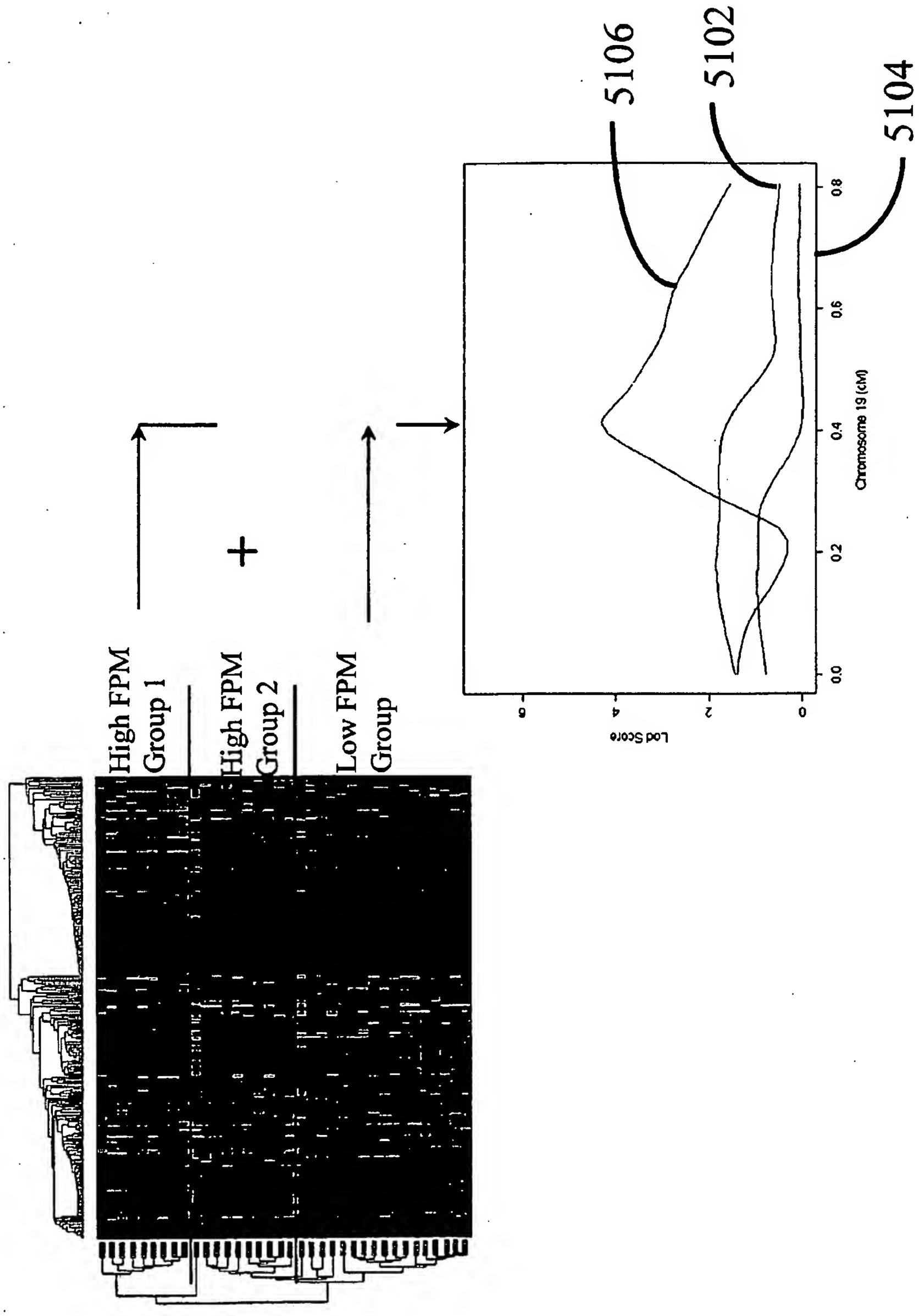
5106
5102
5104
High FPM Group 1
High FPM Group 2
Low FPM Group
+
Lod Score
Chromosome 19 (cM)
0
2
4
6
0.0
0.2
0.4
0.6
0.8

Fig. 51

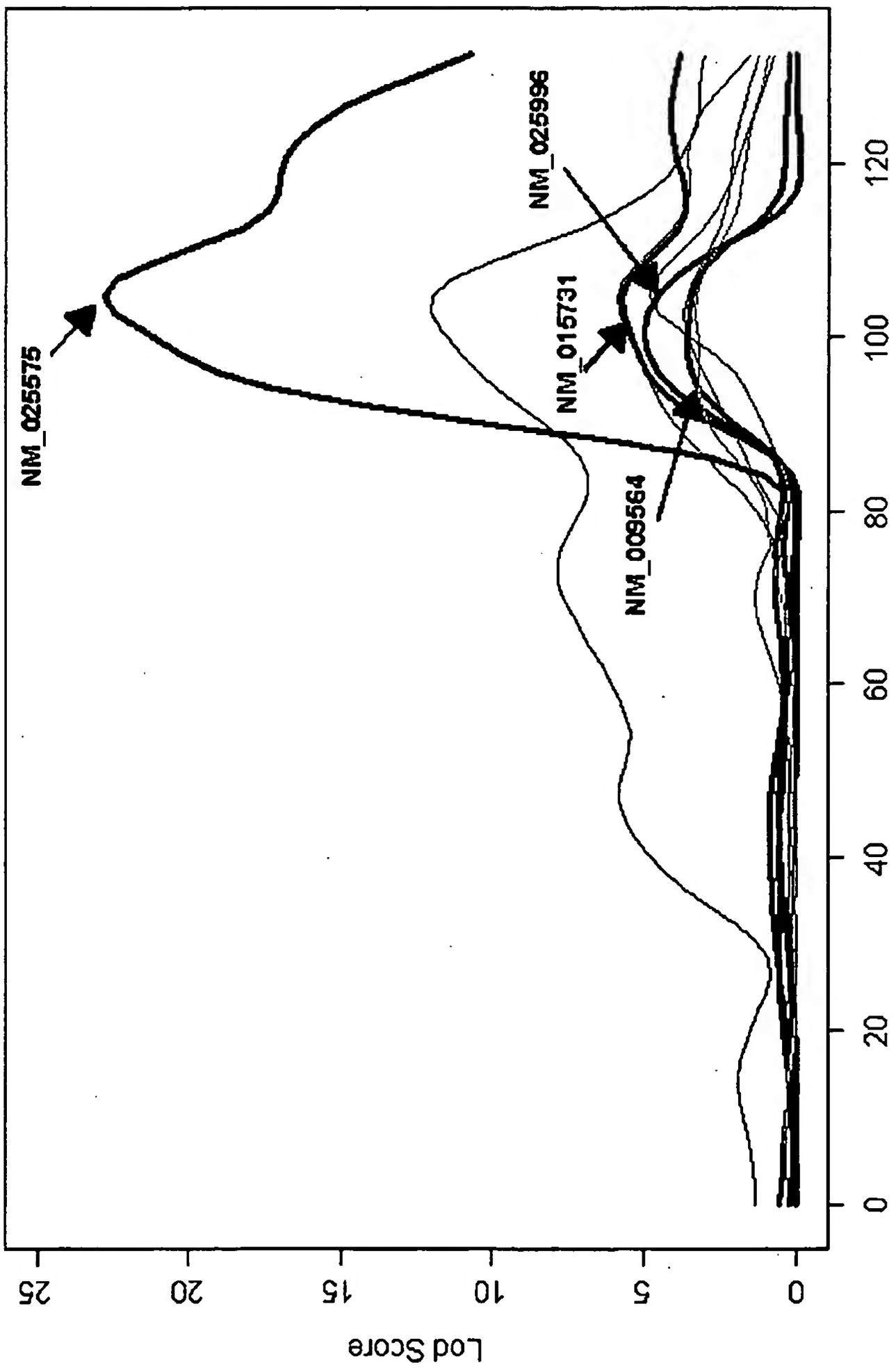
NM_025575
NM_025996
NM_015731
NM_009564
Lod Score
0
5
10
15
20
25
Chromosome 2 (cM)
40
60
80
100
120
0
20

Fig. 52

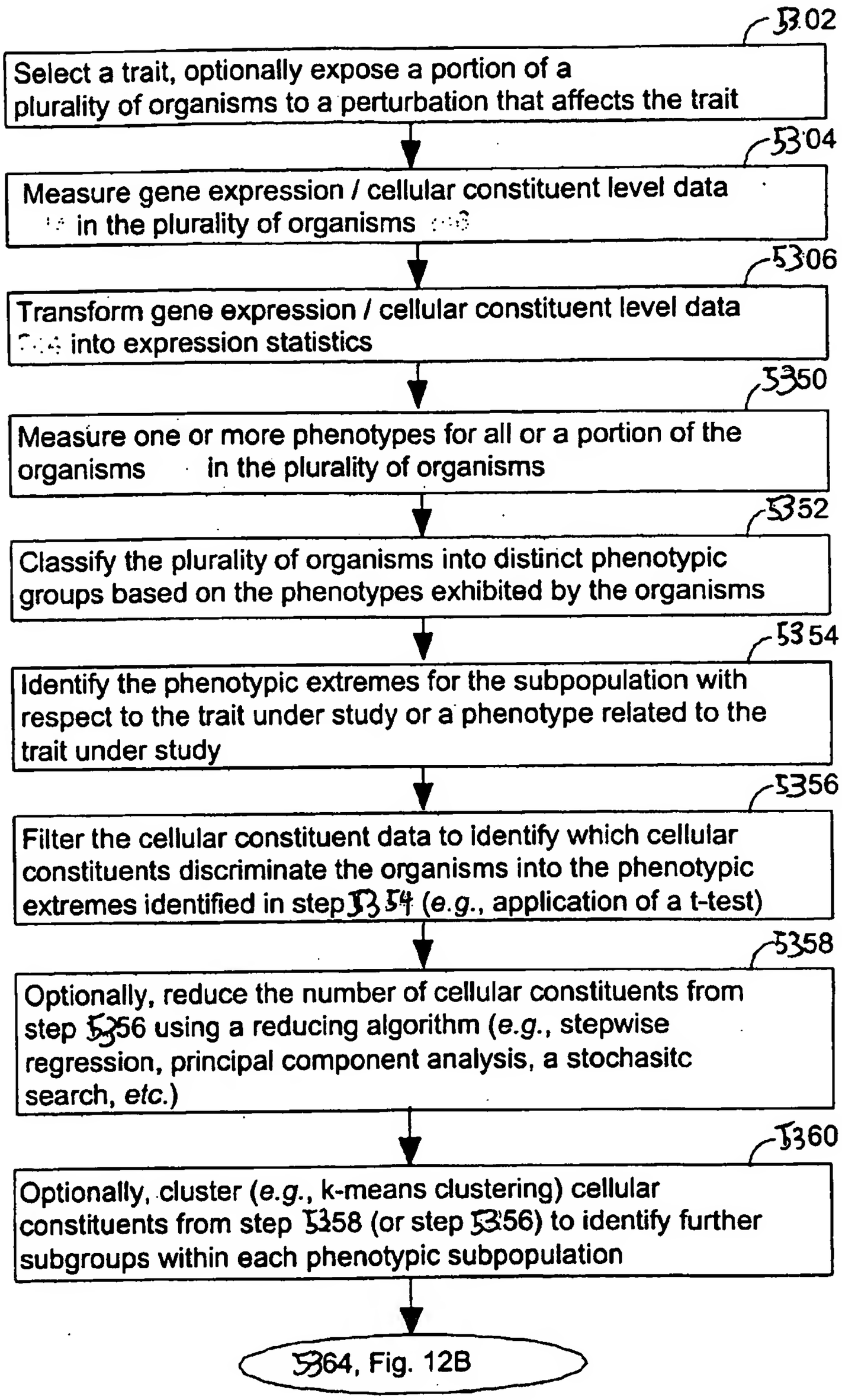
5302
Select a trait, optionally expose a portion of a plurality of organisms to a perturbation that affects the trait
5304
Measure gene expression / cellular constituent level data in the plurality of organisms
5306
Transform gene expression / cellular constituent level data into expression statistics
5350
Measure one or more phenotypes for all or a portion of the organisms in the plurality of organisms
5352
Classify the plurality of organisms into distinct phenotypic groups based on the phenotypes exhibited by the organisms
5354
Identify the phenotypic extremes for the subpopulation with respect to the trait under study or a phenotype related to the trait under study
5356
Filter the cellular constituent data to identify which cellular constituents discriminate the organisms into the phenotypic extremes identified in step 5354 (e.g., application of a t-test)
5358
Optionally, reduce the number of cellular constituents from step 5356 using a reducing algorithm (e.g., stepwise regression, principal component analysis, a stochasitc search, etc.)
5360
Optionally, cluster (e.g., k-means clustering) cellular constituents from step 5358 (or step 5356) to identify further subgroups within each phenotypic subpopulation
5364, Fig. 12B

FIG. 53A

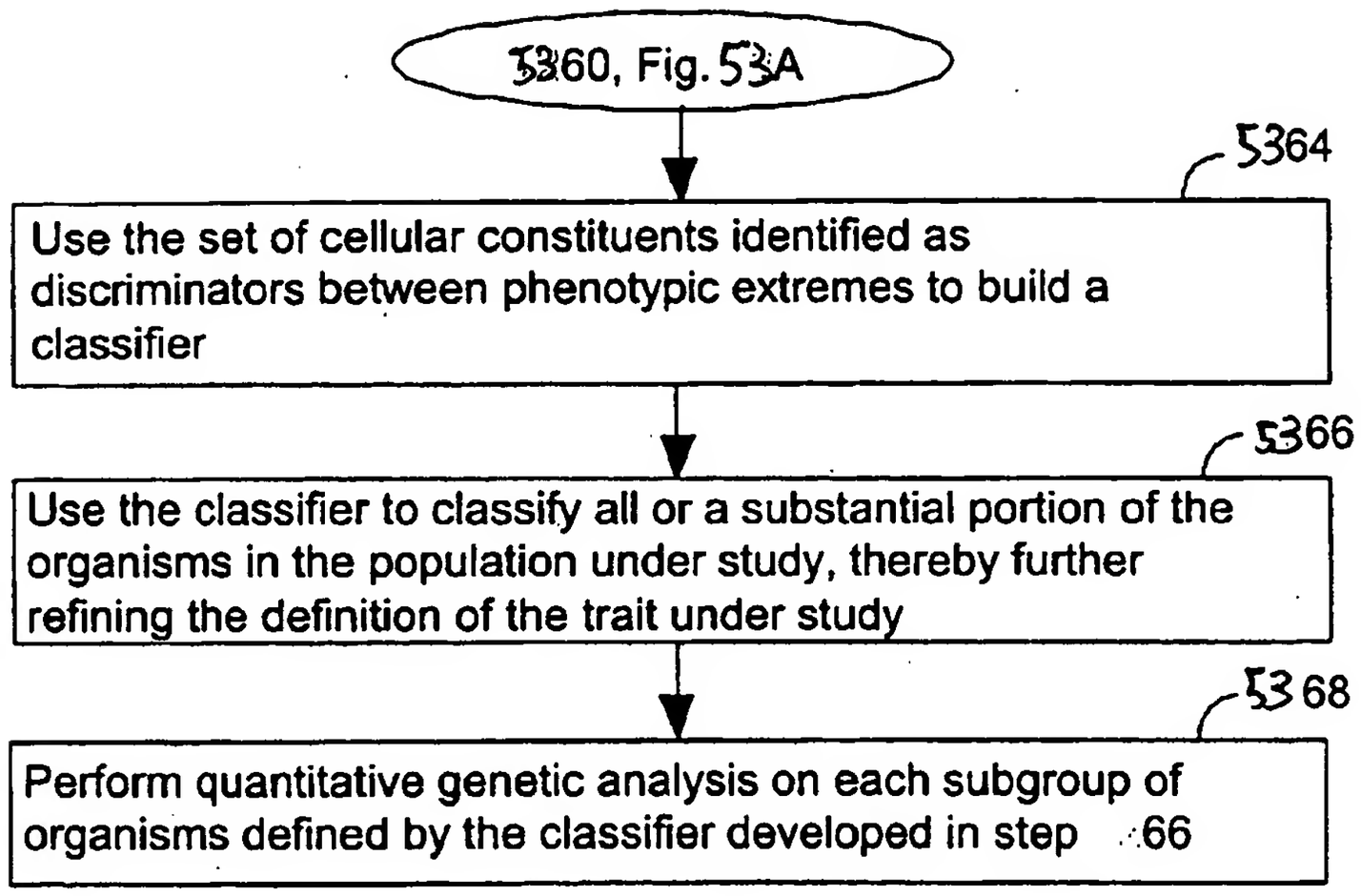
5360, Fig. 53A
5364
Use the set of cellular constituents identified as discriminators between phenotypic extremes to build a classifier
5366
Use the classifier to classify all or a substantial portion of the organisms in the population under study, thereby further refining the definition of the trait under study
5368
Perform quantitative genetic analysis on each subgroup of organisms defined by the classifier developed in step 66

FIG. 53B

	Phenotype 1	...	Phenotype M	CC 248-1	...	CC 248-Z
Organism 46-1	Amount 1301-1-1	...	Amount 1301-1-M	Level 250-1-1	...	Level 250-1-Z
Organism 46-2	Amount 1301-2-1	...	Amount 1301-2-M	Level 250-2-1	...	Level 250-2-Z
⋮	⋮	⋮	⋮	⋮	⋮	⋮
Organism 46-N	Amount 1301-N-1	...	Amount 1301-N-M	Level 250-N-1	...	Level 250-N-Z

FIG. 54

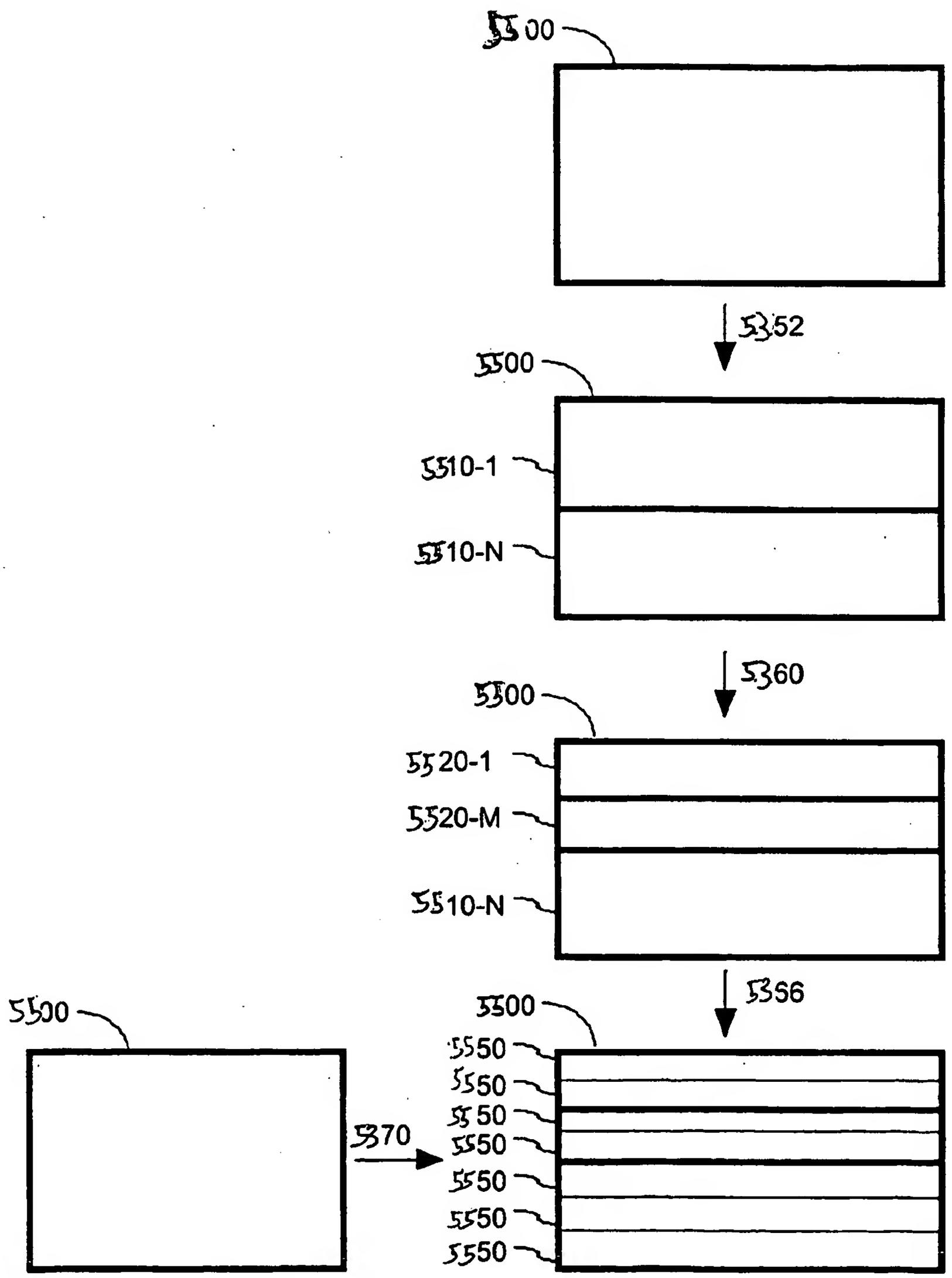
5500
5352
5500
5510-1
5510-N
5360
5500
5520-1
5520-M
5510-N
5356
5500
5550
5550
5550
5550
5550
5550
5370
5500

FIG. 55

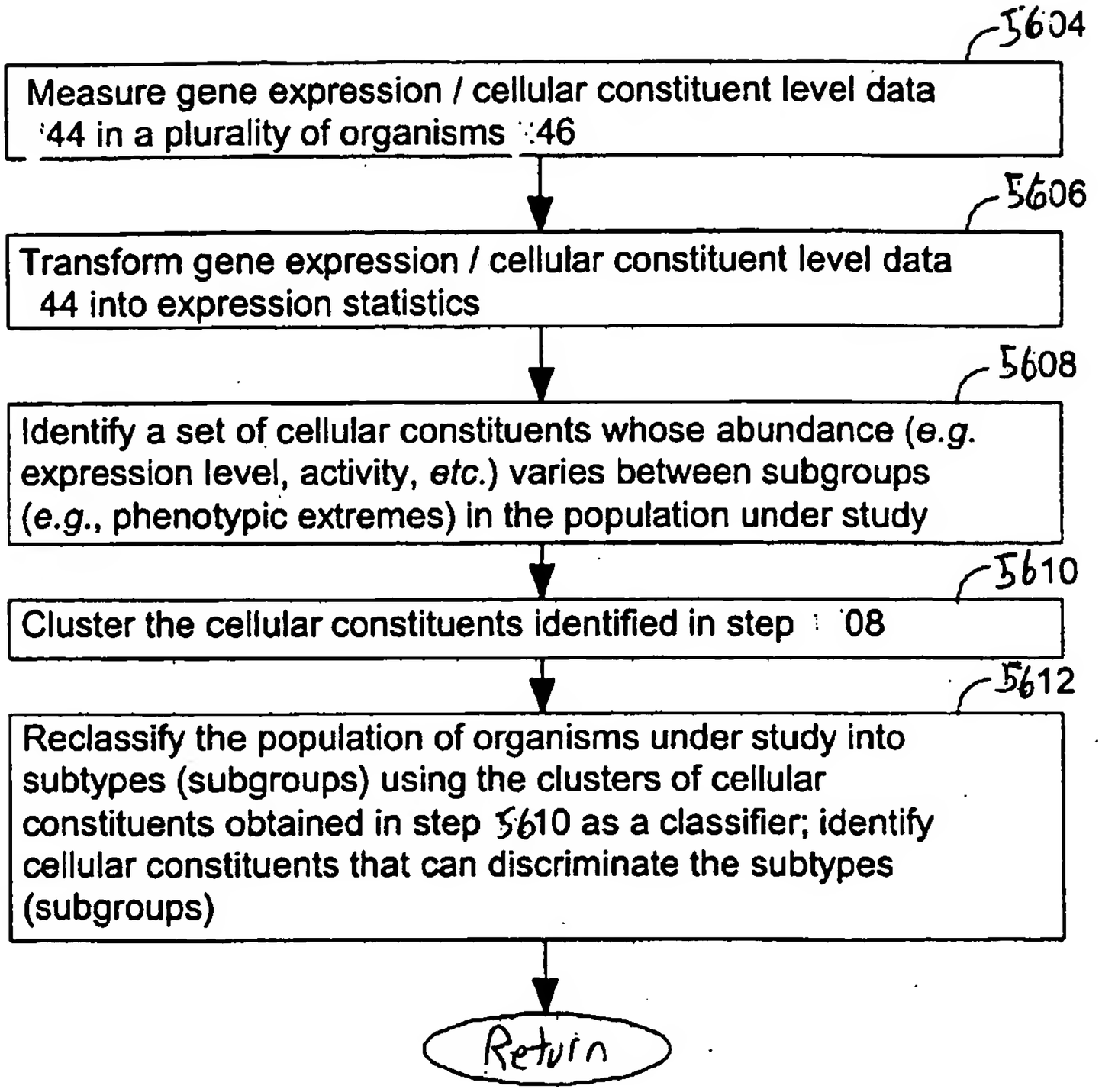
5604
Measure gene expression / cellular constituent level data 44 in a plurality of organisms 46
5606
Transform gene expression / cellular constituent level data 44 into expression statistics
5608
Identify a set of cellular constituents whose abundance (e.g. expression level, activity, etc.) varies between subgroups (e.g., phenotypic extremes) in the population under study
5610
Cluster the cellular constituents identified in step 608
5612
Reclassify the population of organisms under study into subtypes (subgroups) using the clusters of cellular constituents obtained in step 5610 as a classifier; identify cellular constituents that can discriminate the subtypes (subgroups)
Return

FIG. 56